PAPER

Keratoconjunctivitis sicca in dogs under primary veterinary care in the UK: an epidemiological study

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Objectives: To estimate the frequency and breed-related risk factors for keratoconjunctivitis sicca (KCS) in dogs under UK primary veterinary care.

Methods: Analysis of cohort electronic patient record data through the VetCompass Programme. Risk factor analysis used multivariable logistic regression.

Results: There were 1456 KCS cases overall from 363,898 dogs [prevalence 0.40%, 95% confidence interval (CI) 0.38–0.42] and 430 incident cases during 2013 (1-year incidence risk 0.12%, 95% CI 0.11–0.13). Compared with crossbreds, breeds with the highest odds ratio (aOR) for KCS included American cocker spaniel (aOR 52.33: 95% CI 30.65–89.37), English bulldog (aOR 37.95: 95% CI 26.54–54.28), pug (aOR 22.09: 95% CI 15.15–32.2) and Lhasa apso (aOR 21.58: 95% CI 16.29–28.57). Conversely, Labrador retrievers (aOR 0.23: 95% CI 0.1–0.52) and border collie (aOR 0.30: 95% CI 0.11–0.82) had reduced odds. Brachycephalic dogs had 3.63 (95% CI 3.24–4.07) times odds compared to mesocephalics. Spaniels had 3.03 (95% CI 2.69–3.40) times odds compared to non-spaniels. Dogs weighing at or above the mean bodyweight for breed/sex had 1.25 (95% CI 1.12–1.39) times odds compared to body weights below. Advancing age was strongly associated with increased odds.

Clinical significance: Quantitative tear tests are recommended within yearly health examinations for breeds with evidence of predisposition to KCS and might also be considered in the future within eye testing for breeding in predisposed breeds. Breed predisposition to KCS suggests that breeding strategies could aim to reduce extremes of facial conformation.

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INTRODUCTION

Keratoconjunctivitis sicca (KCS) describes a deficiency of the aqueous portion of the tear film that may be primary (e.g. immune mediated) or secondary to systemic diseases or the use of pharmaceutical agents. This condition has been extensively reviewed before (Aguirre *et al.* 1971, Kaswan *et al.* 1987, Kaswan & Salisbury 1990, Sanchez *et al.* 2007, Sansom & Barnett 1985, Williams 2008). KCS is an important ocular condition because it is associated with irritation of the ocular surface in acute and chronic forms, and often leads to corneal ulcerative disease that can be perforating in some cases (Sanchez *et al.* 2007).

The epidemiology of KCS has been described in several publications over the last 50 years (Aguirre *et al.* 1971, Grauwels 1979, Helper 1996, Kaswan & Salisbury 1990, Kaswan *et al.* 1991, Morgan & Abrams 1991, Salisbury *et al.* 1990, Salisbury & Kaswan 1990, Sansom & Barnett 1985). Helper (1996) included 754 referral cases from 13 North American veterinary schools that used the Veterinary Medical Data Program to report predisposition to KCS in several dog breeds spanning a 12-year period (1964–1973). Kaswan and Salisbury (1990) also used the Veterinary Medical Data Program to propose several breed predispositions with data that spanned a 34-year period (1964–1988). The results of these two studies concurred on six breed predispositions: English bulldog, West Highland white terrier, pug, cocker spaniel, pekingese and miniature schnauzer. Other breeds reported as predisposed by one or other study included cavalier king Charles spaniel, Lhasa apso, shih-tzu, blood hound, Boston terrier, Samoyed, Yorkshire terrier and English springer spaniel (Kaswan & Salisbury 1990, Helper 1996). A 1985 study in the UK with 200 referral cases of primary and secondary KCS collected over a 9-year period reported that just over one-third of the cases were West Highland white terriers, suggesting a predisposition in this breed (Sansom & Barnett 1985). A later 2007 study, also from the UK, included 229 referral primary KCS cases spanning an 8-year period and suggested predispositions in English cocker spaniel, cavalier king Charles spaniel, West Highland white terrier and shih-tzu breeds (Sanchez *et al*. 2007). However, the prevalence and incidence risk of KCS in the general population of dogs around the world have remained largely unreported because the aforementioned studies focused on referral rather than primary care practice populations (Bartlett *et al*. 2010). In addition, these previous studies either contained relatively few cases or required a span of several years to capture larger case numbers (Sanchez *et al*. 2007, Sansom & Barnett 1985), sometimes extending to several decades (Helper 1996, Kaswan & Salisbury 1990, Kaswan *et al*. 1991).

Ideal study populations for epidemiological studies that aim to report on disease risk should be large and representative enough to comfortably allow for detection of adequate cases, show variation in the putative risk associated factors and span a short and defined time frame (e.g. 1 year) (Dohoo *et al*. 2009). In addition, there is a growing call for studies that include only primary care cases to avoid a referral bias and to promote generalisability to the wider dog population (Bateson 2010, McGreevy & Nicholas 1999, O'Neill *et al*. 2014a). Unfortunately, until recently, lack of availability of access to clinical data on large enough populations of primary care caseloads has prevented estimation of prevalence and incidence risk for many important disorders such KCS, and consequently many breed-related associations remained unreported. However, in recent times, specialised computer programmes have enabled data sharing into national epidemiological projects from a large number of participating primary-care veterinary practices within a geographical area (PETscan 2020, SAVSNET 2020, VetCompass Australia 2020, VetCompass 2021). In the UK, the VetCompass™ programme collates de-identified electronic patient record (EPR) data on over 15 million companion animals from over 1800 primary-care veterinary practices for epidemiological research (VetCompass 2021).

This study aimed to estimate the frequency of KCS in dogs in the UK using data extracted from a large number of animals under primary veterinary care within 2013 using the VetCompass Programme. The study additionally aimed to evaluate breed and breed-related elements, such as brachycephalia, as risk factors for KCS.

MATERIALS AND METHODS

The cohort of dogs attending VetCompass practices was used to estimate the prevalence, incidence risk and risk factors for KCS during 2013 (Pearce 2012). The sampling frame for the current study included dogs under veterinary care within the VetCompass database from January 1, 2013 to December 31, 2013. Dogs "under veterinary care" were defined as having at least one EPR recorded from January 1, 2013 to December 31, 2013 and/or any dog with at least one EPR both before and after 2013. Sample size calculations estimated that 8625 dogs of a specific breed or group (e.g. brachycephalic or spaniel) and 77,619 dogs that were not of this type would be required to detect an odds ratio (OR) of 1.5 times or greater for KCS assuming a 0.5% prevalence of KCS in the non-type dogs [9:1 ratio of non-type: type, two-sided 95% confidence interval (CI), 80% power] (Epi Info 7 CDC 2019). Ethical approval was granted by the Royal Veterinary College Ethics and Welfare Committee (reference number 2016/U91). Demographic information on each dog was extracted from VetCompass on breed, date of birth, sex, neuter status and bodyweight (O'Neill *et al*. 2014b).

The inclusion criteria for KCS required either a recorded diagnosis of KCS or synonym (e.g. dry eye) and/or at least one Schirmer's tear test-1 <15 mm/minute (or stated to be subnormal) with a concomitant recommendation specifically for topical cyclosporine therapy. Exclusion criteria included dogs that initially met the inclusion criteria but where KCS diagnosis was subsequently recorded as ruled out. For the current study, a KCS case was defined as any dog that met the KCS inclusion criteria described above for a condition that was present during 2013. Case finding involved initial screening of all EPRs of all dogs to identify candidate KCS cases by searching the clinical free text notes field for: "dry eye", kcs*, keratoconj*, keratoconjunctivitis~2, sicca~1, optimmune~1 and the treatment field for: cyclosp*, tacro*, optim*. The EPRs of all candidate cases were manually reviewed in detail to verify case inclusion and the date of first diagnosis was extracted. Confirmed KCS cases were categorised as incident (newly diagnosed during 2013) or pre-existing (first diagnosed before 2013).

Risk factor analysis grouped all dogs with confirmed KCS as *KCS cases* and all remaining dogs as *non-cases*. A *breed* variable included all individual breeds with ≥10 KCS cases or ≥1500 dogs in the overall study to allow focus on commonly affected breed types and to facilitate statistical power for the individual breed analyses (Scott *et al*. 2012). A *purebred* variable categorised currently recognised breeds as purebreds and all remaining types as crossbreds (Dog Breed Info 2019, Irion *et al*. 2003, The Kennel Club 2020b). Purebreds were further categorised by UK Kennel Club breed-recognition (recognised/not recognised) and UK Kennel Club breed group (gundog, hound, pastoral, terrier, toy, utility, working) (The Kennel Club 2020b). Purebreds were also separately categorised based on skull conformation (dolichocephalic, mesocephalic and brachycephalic), spaniel status, poodle status and dachshund status (Appendix S1). Neuter status was defined at the final available EPR. Age was defined as the age (years) at December 31, 2013 and was categorised into five groups: <3.0, 3.0 to <6.0, 6.0 to <9.0, 9.0 to <12.0 and ≥12.0. Adult bodyweight was defined as the mean of all bodyweight (kg) values recorded for each dog after reaching 18 months and was categorised into five groups <10.0, 10.0 to <20.0, 20.0 to <30.0, 30.0 to <40.0 and ≥40.0. The mean adult bodyweight was calculated for all breeds where information available for at least 100 dogs and each dog was categorised as lower than or "at or above" their relevant breed/sex mean bodyweight. This variable allowed the effect of adult bodyweight to be assessed *within* each breed/sex combination (O'Neill *et al*. 2018).

Following data checking and cleaning in Excel (Microsoft Office Excel 2013, Microsoft Corp.), analyses were conducted using Stata Version 13 (Stata Corporation). One-year period prevalence with 95% CIs described the probability of being a KCS case at any time during the 1-year 2013 study period. One-year incidence risk with 95% CIs described the probability of being newly diagnosed with KCS during 2013. The CI estimates were derived from standard errors, based on approximation to the binomial distribution (Kirkwood & Sterne 2003). Descriptive statistics characterised demography separately for the case and non-case dogs. Binary logistic regression modelling was used to evaluate univariable associations between risk factors [*purebred*, *breed*, *skull conformation*, *dachshund type*, *spaniel type*, *poodle type*, *Kennel Club Breed Group*, *adult* (>18 months) *bodyweight* (kg), *bodyweight relative to breed/sex mean*, *age*, *sex and neuter*] and KCS diagnosis. Because breed was a factor of primary interest for the study, *purebred status*, *breed*, *skull conformation*, *dachshund type*, *spaniel type*, *poodle type*, *Kennel Club Breed Group* (variables that are highly collinear with breed) and *adult bodyweight* (a defining characteristic of individual breeds) were excluded from the initial breed-based multivariable modelling. Instead, each of these variables individually replaced the *breed* variable in the final breed-based model to evaluate their effects after taking account of the other confounding variables. Risk factors with liberal associations in univariable modelling (P <0.2) were taken forward for multivariable evaluation. Model development used manual backwards stepwise elimination. Pair-wise interaction effects were evaluated for the final model variables and confounding effects from dropped variables were assessed by individual re-introduction to the final model. Clinic attended was evaluated as a random effect in the final model (Dohoo *et al*. 2009). The area under the receiver operating characteristic (ROC) curve and the Hosmer–Lemeshow test were used to evaluate the quality of the model fit and discrimination (non-random effect model) (Dohoo *et al*. 2009, Hosmer *et al*. 2013). Statistical significance was set at P <0.05. Univariable ORs are reported as OR whereas multivariable ORs are reported as adjusted OR (aOR).

RESULTS

From a study population of 363,898 dogs under primary veterinary care at 300 practices in the UK, there were 1456 KCS confirmed cases during 2013. The 1-year (2013) period prevalence was 0.40% (95% CI 0.38–0.42). Of these prevalent cases, 430 (29.53%) were newly diagnosed during 2013 yielding a 1-year incidence risk of 0.12% (95% CI 0.11–0.13). The breeds with the highest KCS prevalence were American cocker spaniel (5.90%, 95% CI 3.24–8.56), West Highland white terrier (2.21%, 95% CI 1.91–2.50), cavalier king Charles spaniel (1.91%, 95% CI 1.61–2.20), Lhasa apso (1.86%, 95% CI 1.52–2.20), English bulldog (1.82%, 95% CI 1.31–2.32), English bull terrier (1.65%, 95% CI 0.95–2.35) and English cocker spaniel (1.60%, 95% CI 1.38–1.82) (Fig. 1).

Of the prevalent KCS cases with data available for that variable, 1360/1452 (93.66%) were purebred, 723/1453 (49.76%) were female and 916/1410 (64.96%) were neutered. The median adult bodyweight of KCS cases was 11.95 kg [interquartile range (IQR): 9.00–17.80, range: 1.90–82.00), and the median age was 8.98 years (IQR: 6.53–11.75 range: 0.32–19.49). The most common breeds among the KCS cases were West Highland white terrier (n = 212, 14.56%), English cocker spaniel (195, 13.39%), cavalier king Charles spaniel (158, 10.85%), shih-tzu (118, 8.10%) and Lhasa apso (113, 7.76%) (Table 1). Of the 430 incident cases, the median age at first diagnosis of KCS was 7.49 years (IQR: 4.96–10.16, range 0.17–16.45).

Of the non-KCS dogs with data on the variable, 270,955/361,263 (75.00%) were purebred, 174,584/360,411 (48.44%) were female and 184,814/356,814 (51.81%) were neutered. The median adult bodyweight for non-cases was 16.30 kg (IQR: 8.90–27.60, range: 1.00–100.00) and the median age was 3.77 years (IQR: 1.58–7.24, range: 0.00–20.00). The most common breeds among the non-case dogs were Staffordshire bull terrier (26,218, 7.23%), Labrador retriever (24,646, 6.80%), Jack Russell terrier (21,551, 5.95%) and shih-tzu (13,192, 3.64%) (Table 1). Data completeness varied between the variables assessed: breed 99.91%, age 98.33%, sex 99.44%, neuter 98.42% and bodyweight (any age) 88.50% (Fig. 2).

Univariable logistic regression modelling identified 10 variables that were liberally associated with KCS and were further evaluated using multivariable logistic regression modelling: purebred, breed, skull conformation, spaniel type, poodle type, Kennel Club Breed Group, adult (>18 months) bodyweight (kg), bodyweight relative to breed/sex mean, age and neuter (Tables 1 and 2). The final breed-based multivariable model retained three risk factors: breed, age and bodyweight relative to breed/sex mean. No biologically significant interactions were identified in the final model. The final unclustered model showed acceptable model fit (Hosmer–Lemeshow test statistic: P = 0.102) and discrimination (area under the ROC curve: 0.880). The mixed effects model with clinic entered as a random effect was a better model of the data than the fixed effects model (P <0.001) and these mixed effects results are reported. The intraclass correlation coefficient (rho) indicated that 3.03% of the variation in the data was due to clustering at the veterinary clinic level. After accounting for the effects of the other variables evaluated, 22 breeds showed increased adjusted

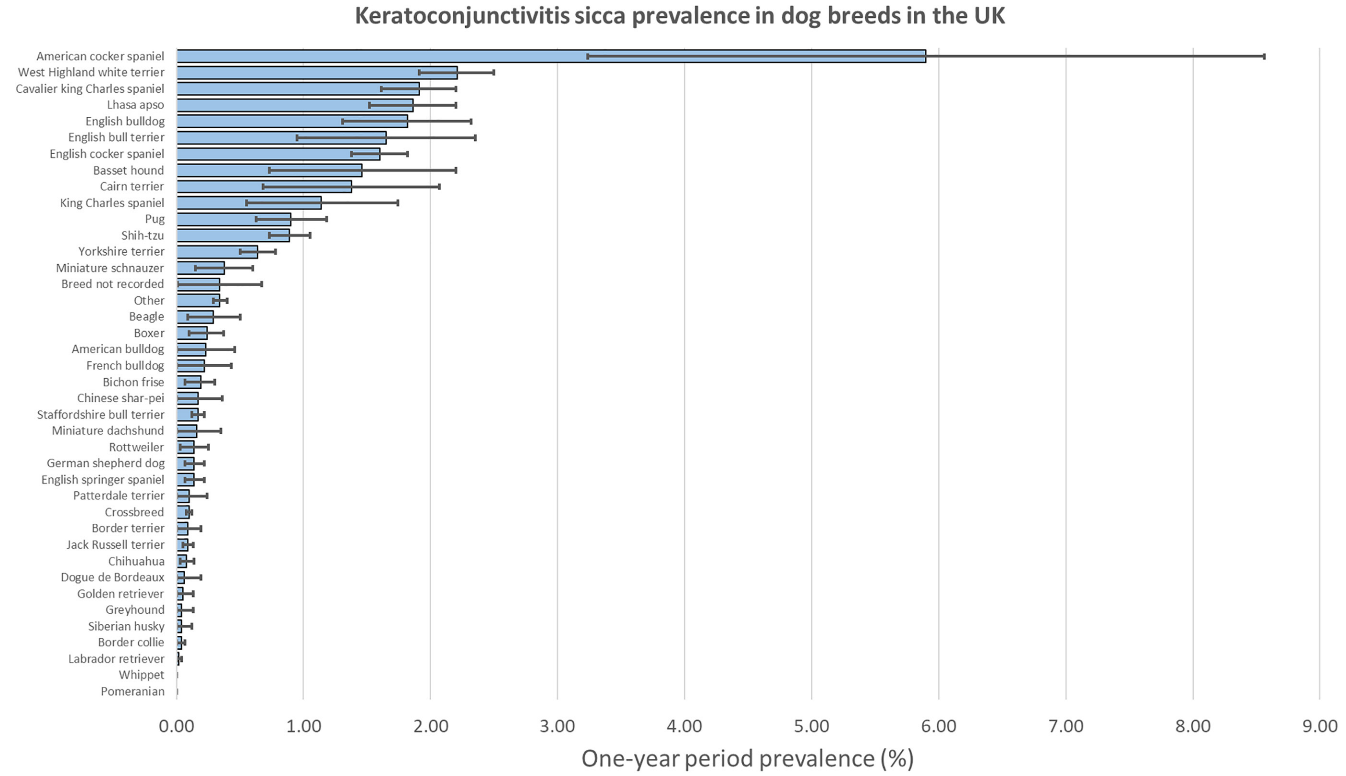

FIG 1. One-year (2013) period prevalence of keratoconjunctivitis sicca in common dog breeds under primary veterinary care in the VetCompass Programme in the UK. The error bars show the 95% confidence interval

odds of KCS compared with crossbred dogs. There were four breeds with an aOR above 20: American cocker spaniel (aOR 52.33, 95% CI 30.65–89.37, P < 0.001), English bulldog (aOR 37.95, 95% CI 26.54–54.28, P < 0.001), pug (aOR 22.09, 95% CI 15.15–32.20, P < 0.001) and Lhasa apso (aOR 21.58, 95% CI 16.29–28.57, P < 0.001). There were a further seven breeds with a high aOR between 10 and 20: cavalier king Charles spaniel (aOR 19.79, 95% CI 15.23–25.71, P < 0.001), English bull terrier (aOR 19.76, 95% CI 12.17–32.08, P < 0.001), English cocker spaniel (aOR 17.76, 95% CI 13.82–22.84, P < 0.001), basset hound (aOR 16.92, 95% CI 9.69–29.52%, P < 0.001), West Highland white terrier (aOR 15.08, 95% CI 11.77–19.3%, P < 0.001), shih-tzu (aOR 13.46, 95% CI 10.2–17.75, P < 0.001) and king Charles spaniel (aOR 12.84, 95% CI 7.25–22.74, P < 0.001). Two breeds showed reduced adjusted odds of KCS compared with crossbreds: border collie (aOR 0.30, 95% CI 0.11–0.82, P = 0.018) and Labrador retriever (aOR 0.23, 95% CI 0.1–0.52, P < 0.001). There were no KCS cases recorded in the Pomeranian and whippet. Dogs that weighed at or above the mean for that breed/sex showed 1.25 (95% CI 1.12–1.39, P < 0.001) times the adjusted odds of KCS compared with dogs that weighed under the mean. Advancing age was strongly associated with increasing adjusted odds of KCS. Compared with dogs aged under 3 years, dogs aged 6.0 to <9.0 years had 11.29 (95% CI 8.8–14.5, P < 0.001) times the adjusted odds and dogs aged ≥12.0 years had 29.44 (95% CI 22.77–38.07, P < 0.001) times the adjusted odds of KCS (Table 3).

After replacing breed from the final breed-based mixed-effects multivariable model, purebred dogs had 5.13 (95% CI 4.15–6.35, P < 0.001) times the adjusted odds of KCS compared with crossbreds. Brachycephalic types had 3.63 (95% CI 3.24–4.07, P < 0.001) times the adjusted odds compared with mesocephalic types. Spaniel types had 3.03 (95% CI 2.69–3.40, P < 0.001) times the adjusted odds compared with dogs that were not spaniel type. Compared with breeds that were not recognised by the Kennel Club, all Kennel Club breed groups except for the pastoral group had higher adjusted odds of KCS. Dogs in lower bodyweight groups had higher adjusted odds of KCS: dogs weighing 10.0 to <20.0 kg had 5.49 (95% CI 4.26–7.08, P < 0.001) times the adjusted odds compared with dogs weighing 30.0 to <40.0 kg (Table 4). Dachshund type and poodle type were not associated with the adjusted odds of KCS following multivariable modelling.

DISCUSSION

A large and representative sample of affected and unaffected animals are needed to report accurately on the prevalence, incidence and risk factors of a disorder, and, ideally, these data should span a period that is as short as possible (Dohoo *et al*. 2009). Achieving such a volume of data to report on relatively uncommon disorders is an arduous task and explains why previous studies of KCS that included over 200 animals required periods from 8 up to 34 years to accrue adequate case numbers (Helper 1996,

Table 1. Descriptive and univariable logistic regression results for breed-related risk factors associated with keratoconjunctivitis sicca in dogs under primary veterinary care during 2013 in the VetCompass Programme in the UK

Variable	Category	Case no. (%)	Control no. (%)	Unadjusted odds ratio	95% CI	Category P-value	Variable P-value
Purebred status	Crossbred	92 (6.34)	90,308 (25.00)	Base			<0.001
	Purebred	1360 (93.66)	270,955 (75.00)	4.93	3.99–6.07	<0.001	
Breed type	Crossbreed	92 (6.34)	90,307 (25)	Baseline	–	–	<0.001
	American cocker spaniel	18 (1.24)	287 (0.08)	61.56	36.66–103.37	<0.001	
	West Highland white terrier	212 (14.6)	9390 (2.6)	22.16	17.34–28.33	<0.001	
	Cavalier king Charles Spaniel	158 (10.88)	8116 (2.25)	19.11	14.76–24.74	<0.001	
	Lhasa apso	113 (7.78)	5961 (1.65)	18.61	14.11–24.53	<0.001	
	English Bulldog	49 (3.37)	2644 (0.73)	18.19	12.83–25.78	<0.001	
	English bull terrier	21 (1.45)	1252 (0.35)	16.46	10.22–26.54	<0.001	
	English cocker spaniel	195 (13.43)	12,011 (3.32)	15.94	12.43–20.43	<0.001	
	Basset hound	15 (1.03)	1011 (0.28)	14.56	8.41–25.22	<0.001	
	Cairn terrier	15 (1.03)	1074 (0.3)	13.71	7.92–23.74	<0.001	
	King Charles spaniel	14 (0.96)	1209 (0.33)	11.37	6.46–20.00	<0.001	
	Pug	41 (2.82)	4507 (1.25)	8.93	6.17–12.92	<0.001	
	Shih-tzu	118 (8.13)	13,192 (3.65)	8.78	6.68–11.54	<0.001	
	Yorkshire terrier	80 (5.51)	12,443 (3.44)	6.31	4.67–8.52	<0.001	
	Miniature schnauzer	11 (0.76)	2922 (0.81)	3.70	1.98–6.91	<0.001	
	Other	128 (8.82)	37,011 (10.24)	3.39	2.60–4.44	<0.001	
	Beagle	8 (0.55)	2727 (0.75)	2.88	1.40–5.94	0.004	
	Boxer	12 (0.83)	5063 (1.4)	2.33	1.27–4.25	0.006	
	American bulldog	4 (0.28)	1716 (0.48)	2.29	0.84–6.23	0.106	
	French bulldog	4 (0.28)	1827 (0.51)	2.15	0.79–5.85	0.135	
	Bichon frise	10 (0.69)	5322 (1.47)	1.84	0.96–3.54	0.066	
	Staffordshire bull terrier	45 (3.1)	26,218 (7.26)	1.68	1.18–2.41	0.004	
	Chinese shar-pei	3 (0.21)	1792 (0.5)	1.64	0.52–5.19	0.398	
	Miniature dachshund	3 (0.21)	1838 (0.51)	1.60	0.51–5.06	0.422	
	German shepherd dog	14 (0.96)	9645 (2.67)	1.42	0.81–2.50	0.217	
	English springer spaniel	13 (0.9)	9049 (2.5)	1.41	0.79–2.52	0.246	
	Rottweiler	6 (0.41)	4376 (1.21)	1.35	0.59–3.08	0.481	
	Patterdale terrier	2 (0.14)	2019 (0.56)	0.97	0.24–3.95	0.969	
	Border terrier	4 (0.28)	4263 (1.18)	0.92	0.34–2.51	0.872	
	Jack Russell terrier	19 (1.31)	21,551 (5.97)	0.87	0.53–1.42	0.566	
	Chihuahua	10 (0.69)	11,955 (3.31)	0.82	0.43–1.58	0.554	
	Dogue de Bordeaux	1 (0.07)	1571 (0.43)	0.62	0.09–4.49	0.640	
	Golden retriever	2 (0.14)	3636 (1.01)	0.54	0.13–2.19	0.389	
	Greyhound	1 (0.07)	2246 (0.62)	0.44	0.06–3.14	0.410	
	Siberian husky	1 (0.07)	2424 (0.67)	0.40	0.06–2.91	0.369	
	Border collie	4 (0.28)	10,640 (2.95)	0.37	0.14–1.00	0.051	
	Labrador retriever	6 (0.41)	24,646 (6.82)	0.24	0.10–0.55	0.001	
	Pomeranian	0 (0)	1711 (0.47)	–			
	Whippet	0 (0)	1691 (0.47)	–			
Skull conformation	Brachycephalic	543 (39.81)	60,570 (21.64)	2.34	2.10–2.62	<0.001	<0.001
	Mesocephalic	715 (52.42)	186,958 (66.78)	Base			
	Dolichocephalic	106 (7.77)	32,435 (11.59)	0.85	0.70–1.05	0.132	
Dachshund type	Not dachshund type	1343 (98.46)	277,544 (98.53)	Base			0.837
	Dachshund type	21 (1.54)	4146 (1.47)	1.05	0.68–1.61	0.836	
Spaniel type	Not spaniel type	947 (69.43)	244,713 (86.87)	Base			<0.001
	Spaniel type	417 (30.57)	36,977 (13.13)	2.91	2.60–3.27	<0.001	
Poodle type	Not poodle type	1344 (98.53)	271,895 (96.52)	Base			<0.001
	Poodle type	20 (1.47)	9795 (3.48)	0.41	0.27–0.64	<0.001	
Kennel Club Breed Group	Not KC-recognised	102 (7.02)	96,730 (26.78)	1			
	Gundog	255 (17.56)	54,920 (15.20)	0.94	0.83–1.07	0.336	<0.001
	Hound	32 (2.20)	12,081 (3.34)	0.83	0.66–1.04	0.11	
	Pastoral	24 (1.65)	23,101 (6.39)	0.53	0.42–0.66	<0.001	
	Terrier	349 (24.04)	68,470 (18.95)	0.89	0.78–1.01	0.061	
	Toy	330 (22.73)	48,939 (13.55)	1.62	1.43–1.84	<0.001	
	Utility	324 (22.31)	37,210 (10.30)	1.12	0.96–1.31	0.156	
	Working	36 (2.48)	19,812 (5.48)	0.33	0.24–0.45	<0.001	

Column percentages shown in brackets.
CI confidence interval.

Kaswan & Salisbury 1990, Kaswan *et al.* 1991, Sanchez *et al.* 2007, Sansom & Barnett 1985). Moreover, application of referral populations will include an inevitable referral bias that limits generalisability to the wider dog population (Bartlett *et al.* 2010). Although each of the aforementioned studies on KCS has been instrumental in building our understanding of

KCS in dogs over the last decades, it is important to expand this knowledge with the inclusion of epidemiological data based on large, primary-care populations of dogs.

The breeds with the highest predispositions (i.e. aORs) in the present primary-care study were American cocker spaniel, English bulldog, pug, Lhasa apso, cavalier king Charles spaniel, English bull terrier, English cocker spaniel, basset hound, West Highland white terrier, shih-tzu and king Charles spaniel. The breed results from the present study and the studies by Sansom and Barnet (1985), Kaswan and Salisbury (1990), Helper (1996) and Sanchez *et al.* (2007) coincide substantially to offer strong evidence for predisposition to KCS in at least six breeds: English cocker spaniel, American cocker spaniel, pug, English bulldog, cavalier king Charles spaniel and West Highland white terrier.

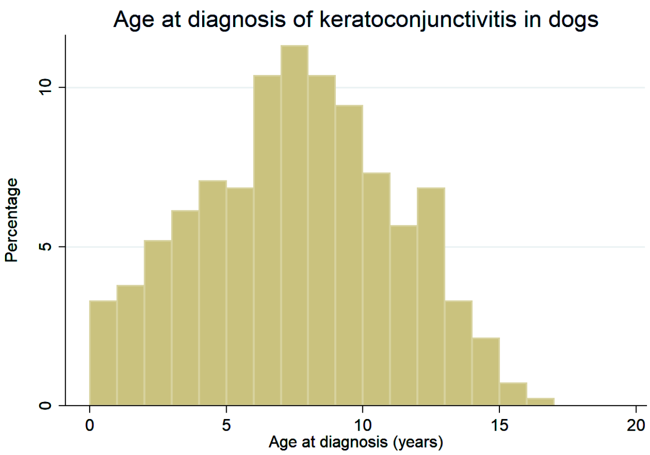

FIG 2. Age at diagnosis of keratoconjunctivitis sicca in dogs under primary veterinary care in 2013 in the VetCompass Programme in the UK. n = 424

Awareness of breed predisposition can be linked to positive actions to mitigate these disorders in commonly affected breeds. For example, a study demonstrated that frequent eye examinations coupled with breeding control strategies were associated with decreased incidence of hereditary cataract and progressive retinal atrophy in dachshunds in Germany (Koll *et al.* 2017). Yet, despite the accumulating evidence of breed predisposition to KCS worldwide, most national eye panels for breeding dogs do not include mandatory quantitative tear testing within their standardised eye examination in any breed. The authors of the present study suggest that inclusion of quantitative tear testing as part of the standardised eye examination of breeding dogs in those breeds with known predispositions to KCS would be sensible to assist with reduction in the incidence of KCS in these breeds. The six breeds suggested by the authors of the present study are ideal candidates to begin this process. It would also appear sensible to recommend consideration of quantitative tear testing in these predisposed breeds within their individual Breed Health And Conservation Strategy Plans that are devised by the UK Kennel Club in conjunction with the relevant breed clubs (The Kennel Club 2020a).

Dogs with acute KCS often present clinically with deep corneal ulceration amid few other clinical signs, prompting a previous recommendation to perform quantitative tear testing in all animals with a history of conjunctivitis, even when patients are young and their clinical signs are mild (Sanchez *et al.* 2007). The findings of the present study show that advancing age was strongly associated with increasing adjusted odds of KCS. This is not surprising if one takes into account that the disease will worsen over time while it remains undiagnosed (Kaswan & Salisbury 1990). Moreover, mean tear readings measured with Schirmer's tear test −1 naturally decrease with age by 0.4 mm/minute for every year

Table 2. Descriptive and univariable logistic regression results for general demographic risk factors associated with keratoconjunctivitis sicca in dogs under primary veterinary care during 2013 in the VetCompass Programme in the UK

Variable	Category	Case no. (%)	Control no. (%)	Unadjusted odds ratio	95% CI	Category P-value	Variable P-value
Adult bodyweight (>18 months) (kg)	<10.0	446 (30.63)	80,584 (22.23)	2.93	2.27–3.80	<0.001	<0.001
	10.0 to <20.0	621 (42.65)	73,254 (20.21)	4.50	3.50–5.79	<0.001	
	20.0 to <30.0	163 (11.20)	53,701 (14.82)	1.61	1.21–2.14	0.001	
	30.0 to <40.0	67 (4.60)	35,555 (9.81)	Base	–	–	
	≥40.0	50 (3.43)	19,814 (5.47)	1.34	0.93–1.93	0.119	
	Unrecorded	109 (7.49)	99,534 (27.46)	0.58	0.43–0.79	<0.001	
Bodyweight relative to breed/sex mean	Lower	623 (42.79)	145,451 (40.13)	Base	–	–	<0.001
	At or above	721 (49.52)	116,998 (32.28)	1.44	1.29–1.60	<0.001	
	Unrecorded	112 (7.69)	99,993 (27.59)	0.26	0.21–0.32	<0.001	
Age (years)	<3.0	78 (5.41)	149,845 (42.05)	Base	–	–	<0.001
	3.0 to <6.0	220 (15.26)	90,609 (25.42)	4.66	3.60–6.04	<0.001	
	6.0 to <9.0	425 (29.47)	58,009 (16.28)	14.07	11.05–17.92	<0.001	
	9.0 to <12.0	387 (26.84)	34,602 (9.71)	21.49	16.84–27.41	<0.001	
	≥12.0	332 (23.02)	23,313 (6.54)	27.36	21.37–35.02	<0.001	
Sex	Female	723 (49.76)	174,584 (48.44)	Base	–	–	0.316
	Male	730 (50.24)	185,827 (51.56)	0.95	0.86–1.05	0.315	
Neuter	Entire	494 (35.04)	171,929 (48.19)	Base	–	–	<0.001
	Neutered	916 (64.96)	184,814 (51.81)	1.72	1.55–1.92	<0.001	

Column percentages shown in brackets.
CI confidence interval.

Table 3. Final mixed-effects breed-based multivariable logistic regression model for risk factors associated with diagnosis of keratoconjunctivitis sicca in dogs attending primary-care veterinary practices in the VetCompass Programme in the UK

Variable	Category	Adjusted odds ratio	95% CI	Category P-value	Variable P-value
Breed	Crossbreed	Baseline			<0.001
	American cocker spaniel	52.33	30.65–89.37	**<0.001**	
	English Bulldog	37.95	26.54–54.28	**<0.001**	
	Pug	22.09	15.15–32.2	**<0.001**	
	Lhasa apso	21.58	16.29–28.57	**<0.001**	
	Cavalier king Charles spaniel	19.79	15.23–25.71	**<0.001**	
	English bull terrier	19.76	12.17–32.08	**<0.001**	
	English cocker spaniel	17.76	13.82–22.84	**<0.001**	
	Basset hound	16.92	9.69–29.52	**<0.001**	
	West Highland white terrier	15.08	11.77–19.3	**<0.001**	
	Shih-tzu	13.46	10.2–17.75	**<0.001**	
	King Charles spaniel	12.84	7.25–22.74	**<0.001**	
	Cairn terrier	9.19	5.28–15.99	**<0.001**	
	French bulldog	8.78	3.2–24.11	**<0.001**	
	Yorkshire terrier	5.25	3.88–7.1	**<0.001**	
	American bulldog	4.93	1.8–13.48	**0.002**	
	Beagle	4.34	2.1–8.98	**<0.001**	
	Miniature schnauzer	4.15	2.21–7.79	**<0.001**	
	Other	3.44	2.63–4.5	**<0.001**	
	Chinese shar-pei	3.07	0.97–9.73	0.057	
	Bichon frise	2.53	1.31–4.87	**0.005**	
	Boxer	2.18	1.19–3.99	**0.011**	
	Chihuahua	2.07	1.08–4	**0.029**	
	Miniature dachshund	1.96	0.62–6.22	0.251	
	Staffordshire bull terrier	1.85	1.29–2.65	**0.001**	
	Rottweiler	1.50	0.66–3.44	0.336	
	Dogue de Bordeaux	1.45	0.2–10.46	0.710	
	German shepherd dog	1.42	0.81–2.49	0.226	
	English springer spaniel	1.26	0.7–2.26	0.434	
	Patterdale terrier	1.09	0.27–4.42	0.908	
	Border terrier	0.91	0.33–2.47	0.849	
	Jack Russell terrier	0.79	0.48–1.29	0.347	
	Siberian husky	0.72	0.1–5.16	0.741	
	Golden retriever	0.41	0.1–1.66	0.210	
	Border collie	0.30	0.11–0.82	**0.018**	
	Greyhound	0.29	0.04–2.08	0.219	
	Labrador retriever	0.23	0.1–0.52	**<0.001**	
	Pomeranian	–	–	–	
	Whippet	–	–	–	
Bodyweight relative to breed/ sex mean	Lower	Base			<0.001
	At or above	1.25	1.12–1.39	**<0.001**	
	Unrecorded	0.51	0.42–0.64	**<0.001**	
Age (years)	<3.0	Base	–		<0.001
	3.0 to <6.0	3.67	2.82–4.77	**<0.001**	
	6.0 to <9.0	11.29	8.8–14.5	**<0.001**	
	9.0 to <12.0	18.85	14.63–24.28	**<0.001**	
	≥12.0	29.44	22.77–38.07	**<0.001**	

The clinic attended was included as a random effect (rho 0.030). P <0.050 shown in bold. N = 363,898.
CI confidence interval.

increase in age (Hartley *et al.* 2006). Based on these findings, the current authors suggest that it would be sensible to extend the recommendation of Sanchez *et al.* (2007) beyond just conjunctivitis to now also recommend that the ocular component within yearly preventive health examinations should include a quantitative tear test in those breeds predisposed to KCS, even for animals without other suggestive clinical signs of KCS.

It has been suggested previously that dogs that present with KCS from breeds with prominent eyes as part of their conformation often also show keratitis in addition to conjunctivitis (Kaswan & Salisbury 1990). Breeds with prominent eyes, such as shih-tzu and cavalier king Charles spaniel, were reported to have a significantly higher risk of corneal ulcerative disease associated with KCS compared to the other breeds in one study (Sanchez *et al.* 2007). Moreover, a recent large study of corneal ulcerative disease in dogs under primary veterinary care in the UK reported that pugs and boxers as well as brachycephalic dogs and spaniels were predisposed to corneal ulceration (O'Neill *et al.* 2017). That paper suggested that breeding reforms that focused on reducing the degree of exaggerated periocular conformation in those breeds might help reduce the incidence of corneal ulcerative disease. The present study reports that small breeds, as well as purebreds, brachycephalic dogs and spaniels, each have a higher risk of KCS. These breed and breed-related risk factors closely overlap with those for corneal ulcerative disease (O'Neill *et al.* 2017, Sanchez *et al.* 2007). Taken together, these findings

Table 4. Results for variables that replaced the breed variable in the final mixed-effects breed-based multivariable logistic regression model for risk factors associated with diagnosis of keratoconjunctivitis sicca in dogs attending primary-care veterinary practices in the VetCompass Programme in the UK

Variable	Category	Adjusted odds ratio	95% CI	Category P-value	Variable P-value
Purebred status	Crossbred	Base			<0.001
	Purebred	5.13	4.15–6.35	**<0.001**	
Skull conformation	Mesocephalic	Base	–	–	<0.001
	Brachycephalic	3.63	3.24–4.07	**<0.001**	
	Dolichocephalic	0.82	0.67–1.01	0.063	
Spaniel type	Not spaniel type	Base	–	–	<0.001
	Spaniel type	3.03	2.69–3.40	**<0.001**	
Kennel Club Breed Group	Not KC-recognised	Base	–	–	<0.001
	Toy	7.92	6.34–9.91	**<0.001**	
	Utility	10.47	8.37–13.11	**<0.001**	
	Terrier	4.38	3.50–5.45	**<0.001**	
	Gundog	4.02	3.19–5.07	**<0.001**	
	Hound	2.50	1.68–3.73	**<0.001**	
	Pastoral	0.83	0.53–1.30	0.427	
	Working	2.07	1.41–3.04	**<0.001**	
Adult bodyweight (>18 months) (kg)	<10.0	4.82	3.70–6.27	**<0.001**	<0.001
	10.0 to <20.0	5.49	4.26–7.08	**<0.001**	
	20.0 to <30.0	1.60	1.20–2.12	**0.001**	
	30.0 to <40.0	Base	–	–	
	≥40.0	1.23	0.85–1.77	0.273	
	Unrecorded	1.51	0.52–4.40	0.451	

Each model also included age and bodyweight relative to breed/sex mean and the clinic attended was included as a random effect. P <0.050 shown in bold.
CI confidence interval.

are strongly suggestive that facial conformations with excessively large interpalpebral aperture, ectropion of the lower eyelid and/or very shallow orbits predispose to corneal ulcerative disease. Therefore, it appears sensible to consider options to breed away from extremes of facial conformation when developing breeding strategies to reduce ocular problems in breeds predisposed to KCS (The Kennel Club 2020a).

The present study identified that dogs weighing at or above the mean for that breed/sex were associated with 1.25 times increased adjusted odds of KCS. It is worth noting that dogs with a bodyweight at or above the mean for their breed/sex are not necessarily overweight/obese, although this may be a contributory factor in some instances. Excess bodyweight has been associated with an increased risk for inherited conditions such as cruciate ligament rupture, hip dysplasia, and hypothyroidism (German 2006, Lund *et al*. 2006, Simpson *et al*. 2019) as well as for certain types of cancer (Weeth *et al*. 2007). Although neutering has often been considered to be associated with subsequent weight gain in dogs, there are still some conflicting results regarding this effect (Reichler 2009). A retrospective study reported increased expression of some heritable conditions in neutered animals but further reported that this effect was not consistent across all heritable conditions (Belanger *et al*. 2017). Another study reported that the association between neutering and the expression of an inherited condition was a direct effect of the neutering and was not due to other factors, such as an alteration of weight metabolism (Oberbauer *et al*. 2019). Although the present study reported an association between bodyweight and increased adjusted odds for KCS, it did not identify any association between neuter status and KCS, or between sex and KCS. A previous study has proposed that a predisposition to KCS in female neutered dogs could be due to the loss of protective hormones (Kaswan *et al*. 1991). However, some studies have failed to identify evidence of a sex predisposition for KCS in dogs (Aguirre *et al*. 1971, Kaswan *et al*. 1985) while another study reported either male or female predisposition to KCS depending on the breed, and that entire (unneutered) animals were more common among cases (Sanchez *et al*. 2007). Given the conflicting results between studies, predispositions to KCS related to sex, neuter status or bodyweight remain difficult to quantify and explain. However, based on the findings of the present study, a sensible approach would be to extend the clinical rationale for the general primary-care recommendation for good bodyweight control by informing owners of a potentially higher predisposition to KCS in small breeds with excessive weight gain (Ward *et al*. 2018).

The application of primary-care veterinary data for epidemiological research has several limitations that have been previously reported (O'Neill *et al*. 2014a, 2019). These include issues related to the re-use of data that were not recorded for research purposes, reliance on accurate note-taking, differing clinical beliefs between clinicians and frequent high levels of missing data. In the specific context of the current study, an additional limitation is that primary care veterinary surgeons may have different levels of experience in the general medicine of ophthalmic practice. Consequently, less experienced veterinarians may be less alert to the clinical presentation of KCS or, conversely, might overinterpret the findings of their ophthalmic examination; either way, this may result in misclassification of KCS cases. Another limitation is that the searching methods used to identify all cases in the current large database depended on the use of key words that could potentially have under-detected true cases. This would have the effect of under-reporting the prevalence and incidence but should not materially affect the identification of the predisposed breeds or other risk factors (Elwood 2007).

CONCLUSIONS

Several dog breeds as well as types of dogs, such as brachycephalic and spaniel types, are predisposed to KCS in the UK. Increased risk of KCS may also be associated with additional factors such as advancing age and weight gain. The authors make recommendations to reduce the incidence and clinical impact of KCS by including quantitative tear tests in eye testing as part of the annual physical examination of all dogs in the list of predisposed breeds, especially as they approach advanced age, and to consider adding it within eye testing for breeding animals as we attempt to gain a more complete understanding of the condition and how it affects these breeds.

Abbreviations

aOR adjusted multivariable odds ratio
CI confidence interval
EPR electronic patient record
ICC intraclass correlation coefficient
IQR interquartile range
OR odds ratio
ROC receiver operating characteristic

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Conflict of interest

The authors declare no conflicts of interest.

Author contributions

All authors made substantial contributions to conception and design, acquisition and extraction of data, and to analysis and interpretation of the results. All authors were involved in drafting and revising the manuscript and gave final approval of the version to be published. Each author agrees to be accountable for all aspects of the accuracy or integrity of the work.

Data availability statement

The data sets generated and analysed during the current study are publicly available on the RVC data repository http://researchonline.rvc.ac.uk/id/eprint/12638/.

References

Aguirre, G., Rubin, L. & Harvey, C. (1971) Keratoconjunctivitis sicca in dogs. *Journal of the American Veterinary Medical Association* **158**, 1566-1579

Bartlett, P. C., Van Buren, J. W., Neterer, M., *et al*. (2010) Disease surveillance and referral bias in the veterinary medical database. *Preventive Veterinary Medicine* **94**, 264-271

Bateson, P. (2010) Independent inquiry into dog breeding. https://dogwellnet.com/files/file/308-independent-inquiry-into-dog-breeding-2010-patrick-bateson/ Accessed November 2, 2020.

Belanger, J. M., Bellumori, T. P., Bannasch, D. L., *et al*. (2017) Correlation of neuter status and expression of heritable disorders. *Canine Genetics and Epidemiology* **4**, 6

Dog Breed Info (2019) Hybrid breeds – list of mixed breed dog. https://www.dogbreedinfo.com/hybridmain.htm. accessed March 23, 2019.

Dohoo, I., Martin, W. & Stryhn, H. (2009) Veterinary Epidemiologic Research. 2nd edn. VER Inc, Charlottetown, Canada

Elwood, M. (2007) Critical Appraisal of Epidemiological Studies and Clinical Trials. 3rd edn. Oxford University Press, Oxford, UK

Epi Info 7 CDC (2019) Centers for Disease Control and Prevention (US): introducing Epi Info 7. https://www.cdc.gov/epiinfo/index.html. Accessed February 14, 2019.

German, A. J. (2006) The growing problem of obesity in dogs and cats. *The Journal of Nutrition* **136**, 1940S-1946S

Grauwels, M. F. M. (1979) A study of keratoconjunctivitis sicca in the dog, unpublished thesis (PhD Thesis), University of Glasgow.

Hartley, C., Williams, D. L. & Adams, V. J. (2006) Effect of age, gender, weight, and time of day on tear production in normal dogs. *Veterinary Ophthalmology* **9**, 53-57

Helper, L. (1996) The tear film in the dog. Causes and treatment of canine keratoconjunctivitis sicca. *Animal Eye Research* **15**, 5-11

Hosmer, D. W., Lemeshow, S. & Sturdivant, R. X. (2013) Applied Logistic Regression. 3rd edn. Wiley, Hoboken, New Jersey

Irion, D. N., Schaffer, A. L., Famula, T. R., *et al*. (2003) Analysis of genetic variation in 28 dog breed populations with 100 microsatellite markers. *Journal of Heredity* **94**, 81-87

Kaswan, R., Fischer, C., Ward, D., *et al*. (1987) Clinical trials of ophthalmic cyclosporine in chronic keratitis. *Transactions of the American College of Veterinary Ophthalmology* **18**, 276-295

Kaswan, R. L., Martin, C. L. & Dawe, D. L. (1985) Keratoconjunctivitis sicca: immunological evaluation of 62 canine cases. *American Journal of Veterinary Research* **46**, 376-383

Kaswan, R. L. & Salisbury, M. A. (1990) A new perspective on canine keratoconjunctivitis sicca. Treatment with ophthalmic cyclosporine. *Veterinary Clinics of North America, Small Animal Practice* **20**, 583-613

Kaswan, R. L., Salisbury, M. A. & Lothrop, C. D. Jr. (1991) Interaction of age and gender on occurrence of canine keratoconjunctivitis sicca. *Progress in Veterinary and Comparative Ophthalmology* **1**, 93-97

Kirkwood, B. R. & Sterne, J. A. C. (2003) Essential Medical Statistics. 2nd edn. Blackwell Science, Oxford

Koll, S., Reese, S., Medugorac, I., *et al*. (2017) The effect of repeated eye examinations and breeding advice on the prevalence and incidence of cataracts and progressive retinal atrophy in German dachshunds over a 13-year period. *Veterinary Ophthalmology* **20**, 114-122

Lund, E. M., Armstrong, P. J., Kirk, C. A., *et al*. (2006) Prevalence and risk factors for obesity in adult dogs from private US veterinary practices. *International Journal of Applied Research in Veterinary Medicine* **4**, 177-186

McGreevy, P. D. & Nicholas, F. W. (1999) Some practical solutions to welfare problems in dog breeding. *Animal Welfare* **8**, 329-341

Morgan, R. & Abrams, K. (1991) Topical administration of cyclosporine for treatment of keratoconjunctivitis sicca in dogs. *Journal of the American Veterinary Medical Association* **199**, 1043-1046

Oberbauer, A. M., Belanger, J. M. & Famula, T. R. (2019) A review of the impact of neuter status on expression of inherited conditions in dogs. *Frontiers in Veterinary Science*, **6**(397), 1-11

O'Neill, D., Church, D., McGreevy, P., *et al*. (2014a) Approaches to canine health surveillance. *Canine Genetics and Epidemiology* **1**, 2

O'Neill, D., Lee, M. M., Brodbelt, D. C., *et al*. (2017) Corneal ulcerative disease in dogs under primary veterinary care in England: epidemiology and clinical management. *Canine Genetics and Epidemiology* **4**, 5

O'Neill, D. G., Church, D. B., McGreevy, P. D., *et al*. (2014b) Prevalence of disorders recorded in dogs attending primary-care veterinary practices in England. *PLoS One* **9**, 1-16

O'Neill, D. G., Corah, C. H., Church, D. B., *et al*. (2018) Lipoma in dogs under primary veterinary care in the UK: prevalence and breed associations. *Canine Genetics and Epidemiology* **5**, 9

O'Neill, D. G., Turgoose, E., Church, D. B., *et al*. (2019) Juvenile-onset and adult-onset demodicosis in dogs in the UK: prevalence and breed associations. *Journal of Small Animal Practice* **61**, 32-41

Pearce, N. (2012) Classification of epidemiological study designs. *International Journal of Epidemiology* **41**, 393-397

PETscan (2020) PETscan. https://www.uu.nl/en/organisation/veterinary-service-and-cooperation/patientcare-uvcu/the-companion-animals-genetics-expertise-centre/projects-and-services/petscan. Accessed March 31, 2020.

Reichler, I. M. (2009) Gonadectomy in cats and dogs: a review of risks and benefits. *Reproduction in Domestic Animals* **44**, 29-35

Salisbury, M., Kaswan, R., Ward, D., *et al*. (1990) Topical application of cyclosporine in the management of keratoconjunctivitis sicca in dogs. *Journal of the American Animal Hospital Association* **26**, 269-274

Salisbury, M. A. & Kaswan, R. L. (1990) Keratoconjunctivitis sicca in dogs. *Veterinary Medicine Report* **2**, 115-127

Sanchez, R. F., Innocent, G., Mould, J., *et al*. (2007) Canine keratoconjunctivitis sicca: disease trends in a review of 229 cases. *Journal of Small Animal Practice* **48**, 211-217

Sansom, J. & Barnett, K. C. (1985) Keratoconjunctivitis sicca in the dog: a review of two hundred cases. *Journal of Small Animal Practice* **26**, 121-131

SAVSNET (2020) SAVSNET. https://www.liverpool.ac.uk/savsnet/. Accessed March 31, 2020.

Scott, M., Flaherty, D. & Currall, J. (2012) Statistics: how many? *Journal of Small Animal Practice* **53**, 372-376

Simpson, M., Albright, S., Wolfe, B., *et al*. (2019) Age at gonadectomy and risk of overweight/obesity and orthopedic injury in a cohort of Golden Retrievers. *PLoS One* **14**, e0209131

The Kennel Club (2020a) Breed health and conservation plans (BHCPs). https://www.thekennelclub.org.uk/health/breed–health–and–conservation–plans/. Accessed November 2, 2020.

The Kennel Club (2020b) Breed Information Centre. https://www.thekennelclub.org.uk/search/breeds–a–to–z. Accessed November 2, 2020.

VetCompass (2021) VetCompass Programme. http://www.rvc.ac.uk/VetCOMPASS/. Accessed February 7, 2021.

VetCompass Australia (2020) VetCompass Australia. http://www.vetcompass.com.au/. Accessed March 17, 2020.

Ward, E., German, A. J. & Churchill, J. A. (2018) The Global Pet Obesity Initiative Position Statement. Available: https://static1.squarespace.com/static/597c71d3e58c621d06830e3f/t/5da311c5519bf62664dac512/1570968005938/Global+pet+obesity+initiative+position+statement.pdf. Accessed May 25, 2021.

Weeth, L. P., Fascetti, A. J., Kass, P. H., *et al*. (2007) Prevalence of obese dogs in a population of dogs with cancer. *American Journal of Veterinary Research* **68**, 389-398

Williams, D. L. (2008) Immunopathogenesis of keratoconjunctivitis sicca in the dog. *Veterinary Clinics of North America: Small Animal Practice* **38**, 251-268

Supporting Information

The following supporting information is available for this article:

Appendix S1. Skull conformation.