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Dogs attending primary-care practice in England with clinical signs suggestive of Chiari-like malformation/syringomyelia

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Abstract

Chiari-like malformation/syringomyelia (CM/SM) in dogs describes a developmental disorder that can cause pain and reduced quality of life. This retrospective study aimed to report the period prevalence, clinical signs and risk factors for diagnosis of symptomatic CM/SM in the veterinary primary-care setting using a cross-sectional design. The study population included all dogs within the VetCompass Programme (01/09/2009-13/06/2014).

Overall, the period prevalence of symptomatic CM/SM was 0.05% (95% confidence interval (CI) 0.04% to 0.06%) for all breeds. The period prevalence in the Cavalier King Charles Spaniel was 1.6% (95% CI 1.2-2.06). Other breeds at increased odds included the King Charles Spaniel, Affenpinscher, Chihuahua and Pomeranian. Insured dogs had 4.6 times the odds (95% CI 2.95-7.17) of having a diagnosis of CM/SM compared with uninsured dogs. Pain was the most common associated clinical sign (67 dogs, 72%). Analgesics were prescribed to 72 (77.4%) of the symptomatic dogs.

Despite its low overall period prevalence, the high proportion of affected dogs identified with chronic pain suggests a significant welfare issue. Financial implications could impede the diagnostic process and lead to under-estimation of the true prevalence. This study may help to inform clinicians about the clinical relevance and the need for improved awareness of clinical signs, particularly in high-risk breeds, to optimise the management of CM/SM in primary-care practice.

Keywords

Epidemiology; Chiari-like malformation; syringomyelia; prevalence; dog; breed; electronic patient record; primary-care; veterinary

Introduction

Canine Chiari-like malformation and syringomyelia are two closely linked conditions that are often recorded as a single entity (Driver and others 2013). Canine Chiari-like malformation (CM) and syringomyelia (SM) may occur independently or concurrently within affected individuals and may manifest symptomatically or asymptomatically (Gamache and Ducker 1990; Parker and others 2011; Plessas and others 2012). CM/SM may be diagnosed as a single entity in primary-care practice (Summers and others 2015) and has been associated with an array of neurological signs that may severely compromise quality of life (Rutherford and others 2012).

Miniaturisation and brachycephaly are reported risk factors for CM (Schmidt and others 2011; Marino and others 2012; Driver and others 2013). CM cases have been reported in many dog breeds with these attributes including the Cavalier King Charles Spaniel (CKCS) (Dewey and others 2005; Rusbridge 2007; Marino and others 2012; Harcourt-Brown and others 2015), French bulldog, Griffon Bruxellois, Chihuahua, Pomeranian, Maltese terrier, Pug and Yorkshire terrier (Marino and others 2012). Prevalence estimates for CM (with or without SM) in the CKCS range from 92-100% (Couturier and others 2008; Cerda-Gonzalez and others 2009). A study of CKCS using magnetic resonance imaging (MRI) screening in the UK and the Netherlands, reported that 25% of CKCS up to the age of 12 months old were reported to have asymptomatic SM, and that 70% of the dogs have developed SM (symptomatic or asymptomatic) by the age of 6 years (Parker and others 2011). However, there are currently few data available on the occurrence of symptomatic CM/SM in dogs presenting to primary-care veterinary practices across all breeds known to be affected.

The most common signs reported for CM/SM are various manifestations of pain, phantom scratching and neurological signs (notably scoliosis, thoracic limb weakness and pelvic limb ataxia) (Rusbridge and others 2006). It is considered that dogs affected by CM/SM experience chronic neuropathic pain which increases anxiety levels and fear-associated behaviour and decreases the quality of life of affected individuals (Rutherford and others 2012). However, no studies to date have described the clinical signs reported for CM/SM cases in dogs presenting in primary-care practice.

The progressive nature of the disease, its frequent severity (Plessas and others 2012) and the high financial burden associated with its diagnosis and treatment can have substantial emotional and economic impact on owners of CM/SM dogs (Shepherd 2008; Franklin and others 2013). Reaching a definitive CM/SM diagnosis can be challenging in primary-care practice. Typical clinical signs overlap with several other disorders and lack specificity, whilst access to MRI imaging facilities may be limited and prohibitively expensive. Conversely, the high proportion of dogs that have CM/SM changes evident on MRI, but appear clinically asymptomatic, frustrates attempts to define the prevalence of clinically affected cases (Rusbridge and others 2006).

This study aimed to (i) report the period prevalence of symptomatic CM/SM diagnosed in primary-care practice in England across all breeds and in CKCS, (ii) describe associated risk factors (including breed) (iii) report the clinical signs shown and treatments prescribed, and (iv) provide information that could lead to improved welfare, emotional and economic impact.

Materials and Methods

The RVC Ethics and Welfare Committee gave ethical approval for this study (ref: URN 2010 1067i). The VetCompass Programme collects primary-care veterinary clinical data (signalment, clinical examination, diagnosis and treatment) from practices throughout the UK (O'Neill and others 2014; VetCompass 2015).

This study interrogated clinical data on all dogs shared with VetCompass from 01/09/2009 to 13/06/2014 which, at that time, covered veterinary practices located across central and southern England (VetCompass 2015). Information collected included patient demographic (species, breed, date of birth, gender, neuter status, colour, insurance status and bodyweight) and clinical information (free-form text clinical notes, VeNom summary diagnosis terms and treatment, with relevant dates) data fields (VeNom Coding Group 2014). Potential CM/SM cases were identified from the free-text and VeNom Code fields using key-search terms (including "*SM*"/"*Chiar*"/"*Syrin*") and were manually reviewed for case inclusion by the first author of the manuscript (veterinary surgeon).

Inclusion as a case required a final diagnosis of CM/SM (or synonym) documented in the veterinary clinical records of a clinically affected dog. The case definition accepted a diagnostic process based on anamnesis and clinical examination and did not mandate any need for MRI. Cases of CM/SM diagnosed using MRI that were asymptomatic or that had signs compatible with CM/SM but that were attributed to alternative concurrent clinical conditions (such as intervertebral disc disease or other neurological problems, dermatological problems, orthopaedic problems) were excluded. Information about clinical signs, treatment received and responsiveness and, as applicable, death, were

recorded. All these features were used for descriptive statistics for welfare, emotional and economic impact.

All dogs in the study population that were not defined as CM/SM cases were included as non-cases for risk factor analysis to investigate the odds of having a diagnosis of CM/SM. Breed, sex, age and insurance status were included in the analysis. Crossbred was considered as control. Insurance status described whether the dog was insured at any point during the study period. Age was defined as the age at first diagnosis for incident cases, or the age at the centre point between the first and final record for the non-cases. No age at diagnosis value was included for pre-existing cases (and so the age of these animals was treated as a missing value). Age was categorised into the four groups used by the British Veterinary Association and the Kennel Club CM/SM Scheme (< 1 year, between 1 and 3 years old, between > 3 and 5 years old and > 5 years) (The Kennel Club 2015a). For CKCS, an additional analysis was carried out within the study population of all CKCS's presenting during the study period and included the above risk factors as well as coat colour (The Kennel Club 2015b).

Considering the expected low prevalence of CM/SM in the general canine population of England, a 'period prevalence' was calculated, which was used to investigate the prevalence of symptomatic CM/SM in dogs diagnosed prior to the study period, as well as those who developed the disease during the period (incident cases). Incident cases were dogs that were first diagnosed with CM/SM during the study period whilst pre-existing cases were defined as dogs first diagnosed prior to the study period.

For incident CM/SM cases, additional information was extracted to compare treatments undertaken and number of visits to assist with estimation of financial and welfare impact: we also noted whether MRI was used during diagnosis, date of diagnosis,

treatment methods, veterinary surgeon prescribing the treatment (i.e. specialist or primary-care veterinary surgeon), referral for specialist care and total number of veterinary visits related to CM/SM during the study period. These data were only collected from incident CM/SM cases because complete clinical records may not have been available in VetCompass for pre-existing cases diagnosed prior to the study period.

Data were exported from the VetCompass database to a spreadsheet (Microsoft Excel 2013 for Windows) for cleaning and formatting. Online software (QuickCalcs, GraphPad Software) was used to calculate 95% confidence intervals (CIs) for prevalence estimates, via a modified Wald method. Data analysis used statistical software (IBM SPSS 21). Demographic variables were explored and described using number and percentage for categorical data and medians (interquartile range (IQR), range) for continuous data. Association between referred cases or those only seen in primary-care practice treatment options, number of drugs used and total number of veterinary visits were evaluated using the chi-squared or Mann Whitney U tests, as appropriate (Field 2013).

Risk factor analysis evaluated associations between demographic variables and the odds of obtaining a diagnosis of CM/SM. Univariate binary logistic regression analysis was conducted and factors with a significance level of $p \leq 0.2$ were added into multivariable logistic regression modelling for further assessment. Model building used manual backwards elimination and the best-fit model was assessed using a likelihood ratio test (Dohoo 2009). Results were considered statistically significant if $p < 0.05$.

Results

The study population included 187,326 dogs with records on the VetCompass database from 01/09/2009 to 13/06/2014 (Figure 1). There were 89,339 females (47.5%), 74,624 dogs were neutered (39.8%), 40,209 were crossbred (54.2%) and 48,119 dogs (25.7%) were insured.

Ninety-three symptomatic CM/SM cases met the case definition, giving a period prevalence overall of 0.05% (95% CI, 0.04%-0.06%). Of these cases, 34 dogs (36.6%) were female, 60 dogs (64.5%) were neutered and 63 dogs (67.7%) were insured.

The most commonly affected breed overall was the CKCS, accounting for 65 (69.9%) of the case dogs (Table 1). Other breeds affected included the King Charles Spaniel (16 dogs, 17.2%), crossbred (3 dogs, 3.2%), Chihuahua, Yorkshire terrier (two dogs each, 2.2 %,) and the Pug, Affenpinscher, Jack Russell terrier, Pomeranian and Shih Tzu (one dog each, 1.1%). Of the three recorded crossbred CM/SM cases, two were recorded as being partly CKCS.

In the 93 cases, the most common sign reported for CM/SM was pain (67 dogs, 72%) (Figure 2). The most common manifestations were phantom scratching (36 dogs, 38.7%), spontaneous yelping (27 dogs, 29%), neck pain on palpation (16 dogs, 17.2%) and provoked yelping, e.g., vocalisation when picked up or touched (15 dogs, 16.1%).

Treatment data were available for 89 of the 93 affected dogs. Seventy two dogs (77.4%) received one or more drugs for treatment of CM/SM, and 17 dogs (20.4%) were un-medicated. Gabapentin, non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids were the most commonly prescribed treatments for CM/SM, administered to 48 dogs (67%), 47 dogs (65%) and 23 dogs (32%), respectively (Figure

3). Of the 17 unmedicated dogs, six were reported to have pain and six were reported to show only scratching behaviour (35.2% each). Of the 72 medicated dogs, 64 (88.8%) were reported to show either a partial or a full response to medication while the remaining nine dogs (12.5%) were reported to have not improved after treatment. Two dogs (2.1% of cases) underwent surgery for CM/SM but the outcomes of surgery were not recorded. During the study period, 23 of the 93 case dogs overall were euthanised/died (24.8%). Of the 93 case dogs, nine (9.8%) died or were euthanised as a result of CM/SM.

Risk factor analysis of diagnosis of CM/SM across all breeds:

Univariable risk factor analysis identified breed, age and insurance as risk factors for symptomatic CM/SM (Table 2).

Multivariable analysis identified three risk factors associated with CM/SM: breed, age and insurance. The CKCS (OR 175, 95% CI 55.14-560.81, $p<0.001$), King Charles Spaniel (OR 226.80, 95% CI 65.82-781.45, $p<0.001$), Affenpinscher (OR 109, 95% CI 5.93-552.59, $p<0.001$), Chihuahua (OR 7.4, 95% CI 1.24-44.71, $p=0.028$) and Pomeranian (OR 14.8, 95% CI 1.54-143.17, $p=0.02$) breeds all had increased odds of diagnosis compared with crossbreds. Dogs aged over five years had 2.7 (95% CI 1.02-7.41, $p=0.045$) times the odds of diagnosis of symptomatic CM/SM compared with dogs of less than one year of age. Insured dogs had 4.6 (95% CI 2.95-7.17, $p<0.001$) times the odds of CM/SM compared with uninsured dogs (Table 2).

Incident cases and comparison between referred and non-referred cases

Incident cases accounted for 48 dogs (51.6%); the remaining 45 dogs (48.4%) had pre-existing records of CM/SM. The median age at diagnosis for the incident cases was 4.25 years (IQR: 2-4.25 years, range 0.21-12.07 years). Of the 48 incident CM/SM cases, MRI had contributed to the diagnostic decision in 36 dogs (75%) (Table 3) while 12 dogs (25%) were diagnosed using only anamnesis, physical exam and radiography. In three of these twelve dogs, radiography was performed to exclude possible orthopaedic disease and discospodylitis. For the incident cases, the number of veterinary visits due to CM/SM during the study period ranged from 1 to 15, with 12 dogs (25%) visiting their primary-care practice on more than seven occasions due to this disorder.

Referred (n=36) and non-referred dogs (n=12) were compared for their first line drug treatment, drugs prescribed and number of visits to the primary-care practice. No significant difference was identified for gabapentin (p=0.082) or NSAIDs (p=0.253) as first drug used between dogs referred and dogs seen only by the primary-care veterinary surgeon. However, the total number of drugs prescribed per dog during the treatment period was significantly higher in referred dogs (median of 2 drugs, range 1-6 drugs) than those not referred (median 1 drug, range 1-2 drugs), (p=0.009). Referred dogs (median 5 visits, range 1-15 visits) also had significantly more veterinary visits to the primary-care practice for CM/SM compared to dogs that were never referred (median 3 visits, 1-10) (p=0.005).

CM/SM diagnosed in the CKCS:

The study included 4,046 CKCSs (2.2% of the overall study population), of which 1,847 (45.7%) were female, 1,910 (47.2%) were neutered and 1,433 (35.4%) were

insured. The coat colour distribution included 1,894 (47%) Blenheim, 559 (13.9%) ruby, 156 (3.9%) black and tan and 1,420 (35.2%) tricolour.

There were 65 CM/SM cases diagnosed in the CKCS breed, giving a period prevalence of symptomatic CM/SM of 1.6% (95% CI 1.2%-2.06%). Of these overall cases, there were 29 (44.6%) females, 42 (64.6%) neutered and 44 (67.7%) insured CKCSs. Among the cases, 34 (52.3%) were Blenheim, 8 (12.3%) ruby, 3 (4.6%) black and tan, and 20 (30.8%) tricolour. During the study period, 11 of the 65 symptomatic CKCS were euthanized/died (27.7%). Nine of symptomatic CKCS (10.8%) died directly as a result of CM/SM.

Univariable risk factor identified that insured dogs had 3.9 times greater odds of diagnosis (OR 3.91 95% CI 2.31-6.60, $p<0.001$) (Table 4). There were no significant associations of sex or coat colour with the diagnosis of symptomatic CM/SM in CKCS. Age group ($p=0.195$), and insurance status ($p<0.001$) were included in the multivariable risk factor analysis. Only insurance was significantly associated with an increased odds of symptomatic CM/SM in CKCS (OR 3.88 95% CI 2.29-6.55, $p<0.001$).

Of the CKCS considered as cases, 29 (44.6%) were incident cases. that showed a median age for diagnosis of 4.5 years (IQR 2.94-6.78 years, range 1.6-11.5 years). MRI was used in the diagnosis of 20 (69%) CM/SM cases while nine (31%) diagnoses did not include MRI.

Discussion

This is the largest epidemiological study to explore symptomatic CM/SM in the general population of practice-attending dogs in England. Analysis of primary-care veterinary data is critically important to assist our understanding of diagnosis, management and clinical impact of CM/SM in the overall canine population and in specific breeds such as the CKCS.

Prevalence of CM/SM in dogs

In the current study, the period prevalence of symptomatic CM/SM reported for all dogs was low in comparison with the most common disorders reported in primary-care practice in dogs (O'Neill and others 2014) where otitis externa, periodontal diseases and anal sac impaction had prevalences of 10.2%, 9.3% and 7.1%, respectively. The large range of breeds included in the study population could explain these figures, as many breeds are not at risk (non-brachycephalic or large breed) of suffering CM/SM.

Underestimation of the true prevalence

Diagnosis of CM/SM generally requires an MRI (Rusbridge and others 2006). However, this is a major limitation in primary-care practice. A significant proportion of dogs in this study were excluded because a clinical diagnosis was not made despite possible signs of CM/SM being present and because clinical signs could be confounded with other diagnosed diseases (Figure 1). This is an important source of underestimation of the true prevalence. It is also a concern as many dogs will not reach a final diagnosis and therefore will not be appropriately treated. This leads to a decrease in welfare of these patients. Some dogs have been diagnosed without MRI and therefore false positives may have been included. Nevertheless, the data provided in this paper reflects how veterinary primary-care practitioners identify and approach these cases,

sometimes without the possibility of reaching a full confirmation with diagnostic imaging.

Owner awareness of normal and abnormal behaviour is also important to detect when their dogs are in pain. The most common clinical signs shown by dogs affected with CM/SM in the current study are similar to previous reports (Rusbridge 2007), although a higher proportion of symptomatic animals were reported to show pain in the current study (72% compared to 35% in previous investigations) (Rusbridge and others 2007). Breakdown of the most common manifestations of pain showed a wide range of non-specific presentations. Further research is needed to elucidate the difference between scratching and pain; the most recent research suggests they are underpinned by separate pathways (Sun and Chen 2007; Rusbridge and Jeffery 2008; Sun and others 2009). However, there is no evidence that scratching is less uncomfortable than pain for these patients. Veterinary practitioners may miss the different manifestations of pain reflected in this paper and described in the literature (Rusbridge and others 2006) if owners do not report this signs as abnormal or disturbing. Therefore, knowledge of the spectrum of behavioural and pain-related clinical signs shown by CM/SM cases could improve diagnosis by increasing awareness in primary-care clinicians of the importance of targeted questioning and history-taking of owners who may even be unaware that these factors are clinically relevant.

The increased diagnosis level recorded in insured animals suggests that financial and other constraints on diagnostic procedures may have allowed the true prevalence of CM/SM in the overall population to be under-estimated. Lack of insurance could potentially lead to fewer dogs being given a final diagnosis of CM/SM especially if dogs other than CKCS show clinical signs associated with this disease complex, where

CM/SM will be in a lower position on (or even absent from) the differential diagnosis list and an MRI may be needed to confirm its presence.

Veterinary clinical data are mainly recorded for clinical use and are not specifically recorded for research purposes. So, a combination of these factors implies that figures reported here are likely to be underestimates of prevalence.

CM/SM diagnosed in the CKCS

The current study identified the CKCS as a predisposed breed (prevalence of CM/SM: 1.6%) in agreement with other studies (Marino and others 2012; Harcourt-Brown and others 2015). The period prevalence of symptomatic CM/SM in CKCS aligns with the results of Summers and others (2015), who reported symptomatic CM/SM in 1.7% of CKCS in primary-care practice. Although a recent study of CKCS reported 15% prevalence for symptomatic CM/SM in Denmark (Thofner and others 2015), the age range it focussed on was restricted to dogs aged over six years whereas the current study included dogs of all ages. However, responder bias in the Danish study could have resulted from some over-reporting of the condition because respondents were asked to volunteer their time to fill-in the questionnaire and it can be assumed that owners with experience and awareness of CM/SM would be more inclined to participate in this kind of study (Thofner and others 2015). Other reports on CM/SM prevalence originate mainly from investigations relying, for definitive diagnosis, on MRI (Parker and others 2011; Thofner and others 2015) among all cases (symptomatic and asymptomatic) rather than records of clinically affected animals from primary-care practice which are the dogs that have compromised welfare. This may help to account for some of the apparent discrepancies because these studies often included asymptomatic animals as cases.

It has been reported that young dogs with asymptomatic SM develop clinical signs later in life (Ives and others 2015), thus increasing the prevalence of dogs with clinical signs in older CKCS. This is in line with our findings, as dogs over five years old had increased odds of having a diagnosis of symptomatic CM/SM in all breeds.

The literature reported CM/SM to be more common in Blenheim and ruby CKCSs, which are recessive coat colours (Rusbridge and Knowler 2004). Nevertheless, the current study failed to identify a significant association between colour coat and symptomatic CM/SM diagnosis. Similarly, age did not statistically affect symptomatic diagnosis in the CKCS, whereas in other studies there was a higher prevalence in dogs older than 3 years of age (Rusbridge 2007; Parker and others 2011). Results of the risk factor analysis in CKCS could be explained by lack of statistical power due to a small sample size, suggesting that even larger studies are needed to more confidently identify risk factors associated with the diagnosis of symptomatic CM/SM in individual breeds.

Although KCS and CKCS are recognised as distinct breeds by the Kennel Club (The Kennel club, 2015b), breed classification in the current study relied on the recorded breed information provided by the owners and veterinary teams as recorded in the clinical notes. Because these two breeds are phenotypically similar, it is possible that some recorded KCS may actually have been CKCS and *vice versa*.

Other breeds affected

The current results from demographic analysis of cases are generally consistent with the affected breeds and age of onset previously reported (Rusbridge and others 2007; Parker and others 2011; Harcourt-Brown and others 2015). The main breeds identified as affected by symptomatic CM/SM in the current study align with those reported in the literature with brachycephalic and miniature breeds being predisposed (Thofner and

others 2015). Risk factor analysis revealed that CKCS, King Charles Spaniel, Pomeranian, Chihuahua and Affenpinscher had increased odds of diagnosis of symptomatic CM/SM compared with crossbreds. Jack Russell Terriers and Yorkshire Terriers, although not identified at increased risk in this study, were also diagnosed. These findings suggest that some breeds other than the CKCS have similar morphological characteristics associated with CM/SM (Marino and others 2012; Cerda-Gonzalez and others 2015). However, Griffon Bruxellois was underrepresented in the current study despite having high CM/SM incidence in other studies (Rusbridge and others 2009; Marino and others 2012). Two of the three crossbreds in the study were partly CKCS, indicating that despite introduction of new genetic material from crossing, causative factors of CM/SM are likely to be inherited (Rusbridge and Knowler 2003; Knowler and others 2016). This information helps veterinary practitioners to consider CM/SM as a differential diagnosis in these breeds when normally it would not have been considered as a possible cause of the clinical signs observed.

Management of CM/SM

This study identified that gabapentin and NSAIDs were the most commonly used treatments for CM/SM. These findings are consistent with published advice that gabapentin is the first line treatment for neuropathic pain with the addition of NSAIDs if there is an inflammatory component (Grubb 2010). Gabapentin and NSAIDs have been recommended specifically to treat neuropathic pain of CM/SM origin (Rusbridge and others 2006), although the efficacy of NSAIDs in controlling pain of CM/SM origin is currently unclear (Rusbridge and Jeffery 2008). The current study failed to identify any statistically significant difference in the usage of analgesics between referred and

non-referred dogs. These results suggest that primary-care veterinary practitioners are closely mirroring the CM/SM treatment protocols of referral practitioners.

Welfare, emotional and economical features

Apart from treatment regimes, management practices differed between dogs that were referred and those that attended only primary-care practice. Referred dogs had more veterinary visits and more drugs prescribed compared with non-referred, possibly because of higher clinical severity in referred dogs. Insured animals had 4.6 times the odds of a CM/SM diagnosis, possibly because of fewer financial restrictions on the use of MRI for diagnosis as well as more frequent veterinary visits and owners arguably having stronger bonds with their dogs (Egenvall and others 2009; Stephens and others 2014). These findings underline the impact of household finance and owner dedication on the diagnosis of CM/SM.

The welfare impact of any condition in a population can be considered in terms of the proportion of individuals affected, but also in terms of the severity and the duration of the challenge experienced by individuals (Collins and others, 2011; Buckland and others, 2014). The mortality results for cases indicated that, although some animals were euthanized on welfare grounds because of CM/SM, a large proportion lived for years with the condition. The percentage of symptomatic dogs in this study that were not receiving any treatment (18.3%) is an interesting finding. Due to the progressive nature of the CM/SM (Plessas and others 2012), it is important that the condition is appropriately managed to maintain the quality of life of affected individuals. Owners of untreated but symptomatic CM/SM dogs may have attributed the clinical signs seen (e.g., phantom scratching) to normal behaviour for the individual or breed and judged it as non-distressing to their pet. Equally, owners may become habituated to

manifestations of pain in their dogs. Thus, educating owners about the likely cause and possible impact on dog welfare of such clinical signs is important to improve diagnosis, especially if MRI is not an option, and ensure effective treatment of any unpleasant sensations (Rutherford and others 2012). All these factors highlight the welfare impact of this complex disorder.

There were some limitations to the current study. Referral institutions normally treat selected diseases associated with more specialised care, representing a source of bias when these data are used for generalizable prevalence estimation (Bartlett and others 2010). On the other hand, epidemiologic data at primary-care veterinary clinics may be unrepresentative by the absence of more severe disease phenotypes or conditions that are diagnosed more commonly at referral clinics (Bartlett and others 2010). However, in most cases, the diagnosis made at the referral centres will still appear in the primary-care records. Breed predisposition leads to the risk of confirmatory bias and dogs classified in this study as a CM/SM case could have been free of CM/SM changes in the MRI.

In conclusion, this study identified that symptomatic CM/SM appears to be a painful disease, with varied clinical manifestations, that persists over time with a low rate of mortality but often demands prolonged poly-pharmacy. A low apparent prevalence of 0.05% symptomatic CM/SM in the overall first opinion population was identified, with many potential reasons of underestimation of the true prevalence. However, a substantially higher apparent prevalence of 1.6% emerged in CKCSs, which in addition to the data showing 72% of affected dogs showed signs of pain, suggests that CM/SM should be considered a disorder of major welfare impact on this breed. Financial limitations complicate a final diagnosis, such that affected dogs may remain untreated.

These results should help clinicians to improve the diagnosis and case management of CM/SM in dogs and may inform control strategies for the disorder in dogs overall and especially in predisposed breeds

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Table 1. Period prevalence of symptomatic CM/SM reported in primary-care veterinary practice in individual breeds of dogs. N/A: not applicable

Breed	Total number of dogs	Number of diagnosed dogs CM/SM cases	Prevalence	Number of cases that included MRI diagnosis
Cavalier King Charles Spaniel	4,046	65	1.6 % (95% CI 1.20-2.06)	36
King Charles Spaniel	871	16	1.84% (95% CI 1.09-3.04)	12
Affenpinscher	235	1	0.4% (95% CI 0.01-2.62)	1
Pomeranian	934	1	0.1% (95% CI 0.01-0.67)	0
Pug	1,726	1	0.06% (95% CI 0.01-0.36)	1
Chihuahua	4,072	2	0.05%(95% CI 0.01-0.19)	1
Yorkshire Terrier	6,299	2	0.03%(95% CI 0.01-0.12)	2
Shih Tzu	3,706	1	0.03% (95% CI 0.01-0.17)	N/A
Jack Russell Terrier	12,024	1	0.01% (95% CI <0.01-0.06)	1
Cross Breeds	40,208	3	N/A	3

Table 2. Risk factor analysis for diagnosis of CM/SM in all breeds of dogs. CKCS: Cavalier King Charles Spaniel; KCS: King Charles Spaniel; * indicates a statistically significant result (p<0.05).

Univariable Binary Logistic Regression Analysis of All Breeds				
Variable	**Categories**	**OR**	**95% CI**	***p* value**
Sex	Female (Base)	1		
	Male	1.58	1.04-2.42	0.324
Insurance Status	Not insured (Base)	1		
	Insured	6.08	3.93 – 9.39	<0.001*
Breed	Cross breed (Base)	1		<0.001*
	Affenpinscher	57.28	5.93-552.59	<0.001*
	Chihuahua	6.55	1.10-39.42	0.039*
	Pomeranian	14.37	1.49-138.21	0.021*
	Pug	7.72	0.80-74.72	0.076
	Shih Tzu	3.65	0.37-34.78	0.266
	CKCS	218.82	68.74-696.52	<0.001*
	KCS	250.71	72.94-862.29	<0.001*
	Jack Russell Terrier	1.18	0.11-10.71	0.925
	Yorkshire Terrier	4.24	0.71-25.47	0.113
	Remaining pure breed	0	0-5.57E+096	0.922
Age group	<1 year old (Base)	1		0.002*
	1 year to 3 years	2.11	0.81-5.52	0.121
	>3 years to 5 years	4.44	1.72-11.17	0.002*
	>5 years	2.93	1.12-7.75	0.027*
Multivariable Binary Logistic Regression Analysis of All Breeds				
Variable	**Categories**	**OR**	**95% CI**	***p* value**
Insurance Status	Not Insured (Base)	1		
	Insured	4.63	2.95-7.174	<0.001*
Breed	Cross breed (Base)	1		<0.001*
	Affenpinscher	109.70	11.25-1069.14	<0.001*
	Chihuahua	7.46	1.24-44.71	0.028*
	Pomeranian	14.86	1.54-143.17	0.020*
	Pug	7.99	0.83-76.93	0.072
	Shih Tzu	3.72	0.38-35.85	0.255
	CKCS	175.86	55.14-560.81	<0.001*
	KCS	226.80	65.82-781.45	<0.001*
	Jack Russell Terrier	1.17	0.12-11.30	0.889
	Yorkshire Terrier	4.49	0.75-26.91	0.100
	Remaining pure breed	0	0-7.55E+092	0.917
Age group	< 1 year old (Base)	1		0.060
	1 year to 3 years	0.88	0.51-1.54	0.674
	> 3 years to 5 years	1.43	0.84-2.39	0.184
	> 5 years	2.71	1.02-7.41	0.045*

Table 3. Descriptive information used in the diagnosis of CM/SM reflecting welfare of dogs, emotional and economic owners' impact (results are based only on dogs where appropriate information was available).

Descriptor	**N of dogs**	**%**
MRI used in diagnosis- referred to specialists (incident cases only)	36/48	75
In pain	67/93	72
On treatment	72/89	80.8
Treated with more than 3 drugs (range= 1-6 drugs)	13/72	18
Non-responders at all to treatment	9/72	10
Un-treated with pain	6/58	10.3
More than 7 visits due to CM/SM (incident cases only, range= 1-15 visits)	12/47	25.5
Died/euthanized due to CM/SM	9/93	9.8

Table 4. Risk factor analysis for diagnosis of CM/SM in Cavalier King Charles Spaniels (CKCS), * indicates statistically significant result ($p<0.05$).

Univariable Binary Logistic Regression Analysis of CKCS				
Variable	**Categories**	**OR**	**95% CI**	***p* value**
Sex	Female(Base) Male	1 1.04	 0.641-1.717	 0.850
Insurance Status	Not Insured (Base) Insured	1 3.91	 2.31-6.60	 <0.001*
Colour coat	Blenheim (Base) Ruby Black and Tan Tricolour	1 0.79 1.07 0.78	 0.36-1.72 0.32-3.53 0.44-1.36	0.807 0.561 0.908 0.385
Age group	<1 year old(Base) 1 year to 3 years >3 years to 5 years >5 years	1 2.86 0.84 1.21	 0.94-8.64 0.44-1.61 0.65-2.24	0.156 0.062 0.603 0.539
Multivariable Binary Logistic Regression Analysis of CKCS				
Variable	**Categories**	**OR**	**95% CI**	***p* value**
Insurance Status	Not Insured (Base) Insured	1 3.88	 2.29-6.55	 <0.001*
Age group	<1 year old(Base) 1 year to 3 years >3 years to 5 years >5 years	1 2.67 0.83 1.19	 0.87-8.13 0.43-1.59 0.64-2.21	0.195 0.084 0.575 0.578

Figure 1. Flow diagram of dogs entered on VetCompass projecting forward to CM/SM case group. Note that there were dogs excluded in the case definition. There were 79 dogs for which CM/SM was within the differential diagnosis of the veterinary surgeon and were considered cases but were excluded because of insufficient evidence. Forty of these occurred with other painful diseases (IVDD, meningitis) or scratching (otitis and dermatological diseases). Six dogs with CM/SM confirmed by MRI were excluded because they displayed signs of pain compatible with intervertebral disc disease seen on MRI.

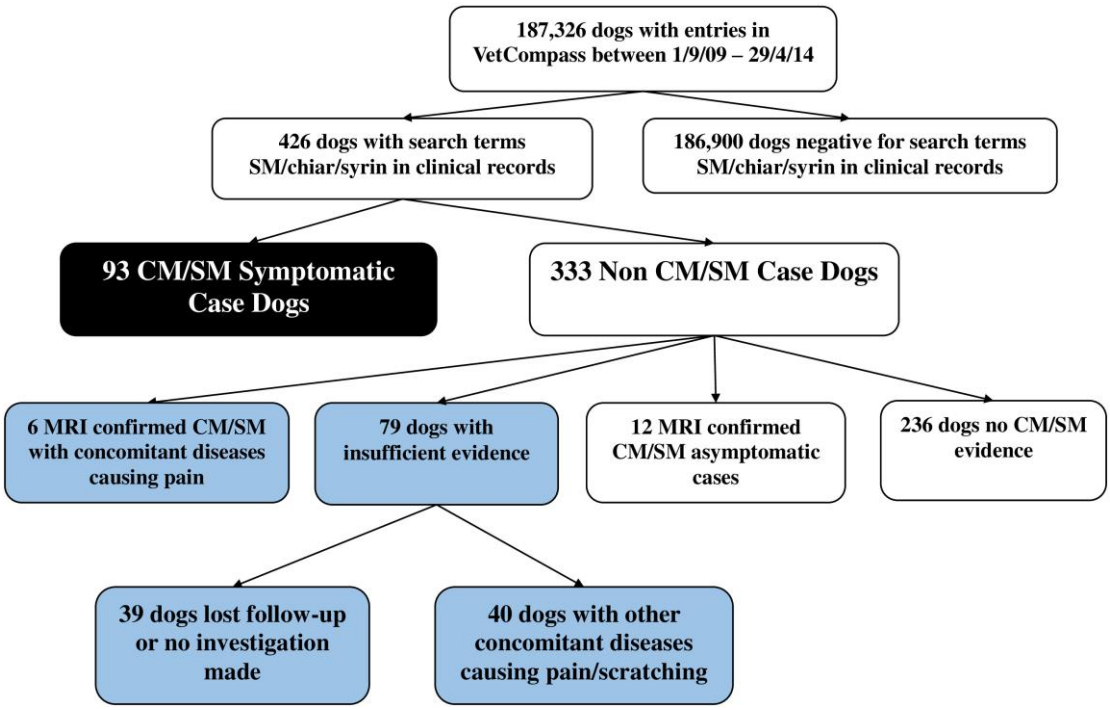

Figure 2. Clinical signs reported in dogs diagnosed with symptomatic CM/SM in primary-care veterinary practice. Signs are organised by main types of clinical signs: scratching (blue), pain (red), neurological signs (green), behavioural changes (yellow) and non-specific (black).

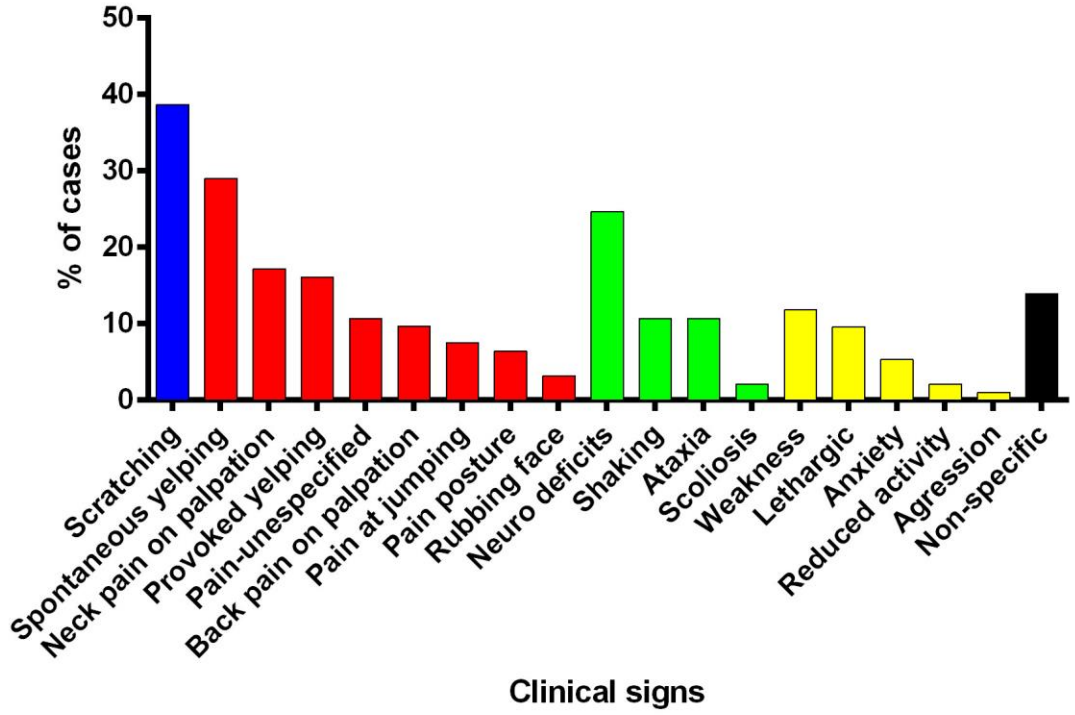

Figure 3. Proportion of drugs prescribed to symptomatic CM/SM cases diagnosed in dogs attending primary-care veterinary practice in England. Dogs might receive more than one treatment.