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# Epidemiological Investigation into Canine Osteoarthritis and its Associated Conditions, and the Associated Pain Related Behaviours in the UK Dog Population

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# EPIDEMIOLOGICAL INVESTIGATION INTO CANINE OSTEOARTHRITIS AND ITS ASSOCIATED CONDITIONS, AND THE ASSOCIATED PAIN RELATED BEHAVIOURS IN THE UK DOG POPULATION

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Canine osteoarthritis (OA) is a progressive and chronic disease that results in the destruction and deterioration of the cartilage surrounding synovial joints. It frequently presents with pain and lameness in dogs and can result in euthanasia. However, the pathogenesis and epidemiology of OA is poorly described in current literature. The aim of this study was to identify epidemiological information of OA such as the prevalence, severity, duration and risk factors contributing to the development of canine OA. This study also aimed to investigate how frequently relevant behavioural signs are recorded in primary care consultations and what pain-related behaviours dogs with OA exhibit. Firstly, the scientific literature was systematically searched following PRISMA (2009) guidelines, to produce a systematic review and meta-analysis on the risk factors that contribute to OA and its predisposing conditions. The second study included a cohort epidemiological study using primary care data from the VetCompass database combined with a case-control risk analysis to support the systematic review. In total forty-four papers were included in the final corpus of the systematic review, and four datasets were included in the meta-analysis. For the cohort study overall, 455,557 dogs were included in the study as a denominator population. 16,437 candidate OA cases were identified, of which 6102 (37%) were manually checked and 4196 were confirmed as osteoarthritis cases. The main findings in the systematic review showed OA is largely a genetic disorder exacerbated through lifestyle. The meta-analysis results showed females had greatest odds of developing cruciate ligament diseases (fixed effect odds (FE) 1.715, 95% confidence intervals (CI) 1.31 to 2.24; random effect odds (RE) 1.600, 95% CI 1.10 to 2.33) and hip and elbow dysplasia (FE 1.173, 95% CI 0.978 to 1.407; RE 1.129, 95% CI 0.777 to 1.640), and that males have greatest odds of developing OA (FE 2.489 95% CI 1.253 to 4.943; RE 2.274 95% CI 0.707 to 7.309). In the epidemiological study an estimated prevalence for OA was calculated at 2.5%, and average duration of OA was found to be 2 years, presenting for 11% of life. The average severity was 6 (range 13), with obesity ($p<0.001$) and duration ($p=0.018$) significantly affecting severity score. 19.6 % of cases had at least one behavioural problem reported in the EPR, with the top 3 behaviours being dog is quieter, reluctance to exercise and alteration to normal behaviour. The main risks found in the risk analysis were age, insurance status and breed group (all $p<0.001$). This shows OA affects thousands of individuals and can have an incredibly long duration. It also showed that behaviour discussions were recorded in just under a fifth of cases. Further investigations are warranted in order to support this study as well as to reduce the number of cases of OA, as this disease can seriously impact canine welfare.

# Table of Contents

# Chapter 1

## Introduction

### Epidemiological investigations and their importance

Epidemiological investigations play an important role in both human and veterinary medicine, studying particular diseases within a certain population. These types of studies allow for prevalence estimates, disease prioritisation, severity and duration estimates, as well as identifying the risk factors that increase the likelihood of disease in order to allow for optimum treatment, prevention and control. They also improve our understanding of disease aetiology, which again is vital for control and prevention. These studies are common in human medicine and are becoming increasingly so in veterinary medicine in all fields. Veterinary studies are also an important contributor to public health, through the areas of zoonotic infections, medical research and animal health itself (Sargeant, 2008). The recent increasing interest in One Health, (an inter-disciplinary collaboration between the Food and Agriculture Organization, the World Health Organization, and the World Organisation for Animal Health) has potentially highlighted the role of dogs in human health (Gibbs, 2014). It has been suggested that while dogs can strongly help the support of, and also recovery from an ailment, ownership of a dog may also actually reduce illness both physically and psychologically in some cases. It has also been found that dogs can be used to detect a variety of ailments such as seizures, cancers, and hypoglycaemia, as well as provide relief to families with children with autism and are therefore very important in human medicine (Hall et al., 2016 and Wells, 2007). Whilst these human-centric influences may act as a driver for animal studies, the key importance of animal health and welfare epidemiological studies is to predict, monitor and assess risk of welfare or health problems in animals.

A recent UK dog population survey showed that forty percent of UK homes own a pet, a quarter of which own a dog. The dog is the UK's favourite pet with an estimated 8.5 million dogs owned (PFMA, 2016). Therefore, dog health studies are increasingly important. As a result of current and recent breeding practices, a reduction in dog health and welfare has occurred, prompting numerous studies into inherited defects of purebred dogs (Collins et al., 2011 and Summers et al., 2010). It was found that fifty of the most popular breeds owned in the UK have a predisposition to at least one inherited health defect (Asher et al., 2009). This strongly warrants further research into a range of health disorders in order to reduce their impact on dog health and welfare.

Risk factor analysis is an important epidemiological tool. Evaluating the role of 'exposures' in the development of a disease allows the identification, characterisation and quantification of risk factors that can potentially be controlled to prevent future cases of disease, and thus lower its welfare impact on a population (Blumenthal et al., 2001). Another measurement of welfare risk assessment is the Welfare impact (WI). This can be calculated for dog health disorders in order to determine the overall impact on welfare the disorder poses using the prevalence estimate and severity of a disorder, in order to improve current management and strategies ultimately aiming to improve health and welfare. Calculation of welfare impact requires estimates of prevalence and severity to be made (WI= prevalence x severity) (Collins et al., 2010).

Currently, there is a distinct absence of reliable prevalence data for many veterinary diseases and disorders, which makes the task of calculating reliable figures for the welfare impact of a disease on a population difficult. The prevalence of a disease is defined as the number of affected individuals within a population. A previous study has shown that only 1% of inherited canine diseases in the UK have published prevalence data (Collins et al., 2011). In

recent years, a number of projects have been established to attempt to collect data on a large-scale, direct from veterinary practices. These projects, which in the UK include VetCompass[1] and SAVSNET[2], ultimately allow for more accurate calculations of prevalence (O'Neill et al., 2014).

Severity of a disease is another measure that can be used to show the impact of a disease on canine welfare. However, as a measurement it has a certain level of difficulty as methods of calculation are often subjective or use generic scales that may have aspects that are unrelated to particular diseases. Often these are stand-alone scales/scoring systems such as the General Illness Severity Index (GISID) (Asher et al., 2009), quality of life questionnaires (Freeman et al., 2005 and Wiseman-Orr et al., 2006), and pain assessment scoring systems such as the Canine Brief Pain Inventory (CBPI) (Brown et al., 2013). These scales are all very different to one another, and assess various aspects relating to the studied disorder. However, what they do have in common is the use of assessing deviations from the 'norm', which is where the individual is considered fit and healthy. Again, there is difficulty in this due to the lack of knowledge on pain experience in animals, and the variation in what the person assessing considers the 'norm', which could potentially be not healthy and fit at all (Packer et al., 2012).

Measuring duration provides another dimension in the characterisation of a disorder. In some diseases this is an easy measurement to make, such as acute disorders where there is a clear date of onset and end date. However, other disorders pose a greater difficulty, particularly chronic disorders where aetiology and pathological changes are not clear and can be gradual or have recurrent episodes. There is also difficulty at an individual level, where it has been shown that pain expression differs with individual personality and therefore displaying of

[1] See: http://www.rvc.ac.uk/VetCOMPASS
[2] See: https://www.liverpool.ac.uk/savsnet/

signs of disease s at the onset of disease may differ significantly from one individual to the next and therefore not be recognised as the onset (Ijichi et al., 2014). In these cases, duration is more easily defined as time since diagnosis was made by the health-care professional (Davis et al., 2006), however this is not always completely reliable and there is risk of ambiguity, as the diagnosis may not actually be made until much later in disease progression. Duration estimates also depend upon the data provided and can vary greatly, particularly with primary care data, due to differences in duration from first signs shown by the individual to first signs witnessed by the owner to the actual date of diagnosis.

**Association of Pain-Causing Conditions and Behaviour**

Behaviour is currently a primary indicator of pain in veterinary medicine (Epstein et al., 2015). Pain-causing health conditions are frequently associated with the performance of pain behaviours and so behaviours can be used to indicate level of pain severity, though this may be unreliable, as pain expression has been shown to vary with individual temperament (Ijichi et al 2014) Additionally, studies have shown that pain expression also varies with signalment factors such as age, sex and breed (Mathews et al., 2014). These behaviours may be exacerbated by stressors such as anxiety or fear, associated with the experience of pain.

Behaviours seen as a result of pain include aggression, avoidance, attention-seeking behaviour, change in activity levels, and change in vocalisations (Epstein et al., 2015). For example, animals with debilitating diseases may show a decrease in vocalisations and show reluctance to move and therefore decreased activity (Epstein et al., 2015). Due to the nature of chronic diseases, behaviours associated with chronic pain are often subtle and slow to develop and therefore detection is more difficult. It is valuable to know the dog's 'normal' behaviour and to recognise pain as the cause of any change (Mathews et al., 2014), as often euthanasia can result in behaviour cases. Studies are needed to identify particular behaviours

that can be associated with particular diseases so that practitioners can offer behavioural treatment as well as physical treatments, and their recognition can act as educational tools for owners recognising these behaviours in their dogs, as these are often the most likely people to identify an initial problem.

**Canine Health and Inherited Disorders**

After recent criticism of current breed standards and breeding practices, it has been brought to light that many breeds are predisposed to inherited defects. Breed conformation results in disorders in the majority of canine body systems, including cardiovascular, musculoskeletal, respiratory, immunological, gastrointestinal, endocrine, integumentary, urogenital and nervous / sensory (Asher et al., 2009). Dogs commonly suffer from a range of painful disorders linked in part to conformation and genetics, but also exacerbated through environmental factors. The musculoskeletal system is one of the most frequently affected systems, with large numbers of dogs experiencing varying levels of pain associated with conditions affecting this system (Johnson et al., 1994). Musculoskeletal disorders, whilst usually not immediately life threatening, can be extremely debilitating and chronic in duration and therefore significantly impact canine welfare, and can play a role in decisions on euthanasia.

**Canine Osteoarthritis**

Osteoarthritis (OA) is a well-known musculoskeletal condition seen in a wide range of species, from humans (Felson et al., 2000) to companion animals ranging from dogs to guinea pigs (Silverstein and Sokoloff, 1958). Often, OA develops from inherited disorders such as hip/elbow dysplasia and patellar luxation and so a strong link can be made to its development from genetic predisposition (Smith et al., 2001). Canine osteoarthritis occurs within the synovial joints, when the process of cartilage degeneration occurs at a faster rate

than the processes of regeneration and synthesis. It is chronic and progressive in nature, this ultimately results in degradation within the joint, accompanied by changes within the bone and formation of osteophytes (Alam et al., 2011). OA can arise in any joint but most commonly occurs in the hips, elbows, and stifles. It is often associated with particular breeds and with older age, however, it can occur in any individual. OA is chronic and once a diagnosis is made, the condition is present until end of life. There is currently no curative treatment, so the focus is on palliative care and condition management. These include weight and diet management, pain relief and structure modifying treatments (such as cartrophen) (Pettitt and German, 2015). Due to the lack of published epidemiological research on this debilitating condition, further investigation is needed for canine OA and therefore is the focus of this study.

Hip and elbow dysplasia, cranial cruciate ligament rupture and patellar luxation are extensively discussed within the literature. It is frequently noted that these arthropathies often result in the development of OA due to the degradation of the joints each of the diseases presents within (Henrotin et al., 2005). Therefore, these conditions are included in the systematic review in chapter 2, as they are considered a risk for developing OA. Within the current literature other risks linking to the development of OA are explored and range from exercise and diet (Smith et al., 2006) to genetics as well as incorporating signalment aspects (Hays et al., 2007). Many studies investigate a particular risk only and therefore a full review of current risk factors for both OA and its predisposing condition is needed.

Whilst it is discussed in current literature, prevalence estimates for OA vary widely and in the UK have been quoted from 6.6% (O'Neill et al., 2014) up to 20% (Johnston, 1997) in dogs >1 year of age. It is obvious there is a large range of uncertainty in the actual prevalence rate of OA in the UK dog population and therefore this investigation aims to address this gap.

Due to the nature of OA, previously mentioned severity scales (Asher et al., 2009) are not suitable for its assessment and so development of an OA severity scale is needed. Creating a scale for use within this study will be a secondary aim. Longitudinal studies have found OA duration can be long ranging, some studies show that it may first be present in young individuals (Smith et al., 2006).This study intends to use primary-care data in order to provide duration estimates and calculate percentage of life affected.

Previous studies have reported behaviours related to OA using the CBPI (Brown et al., 2013). Both physical and psychological aspects of animal health and welfare should be taken into account when diagnosing and therefore it is important to understand the behaviours that exhibit with particular diseases. It has been discussed that during primary care consultations, behaviour is not talked about enough (Roshier and McBride, 2013a) and therefore this investigation is set out to determine the level of discussion of behaviour in primary care consultations as well as to identify the most frequently observed behaviours associated with OA.

**Study Aims and Objectives**

The aims of this investigation are to generate accurate epidemiological data on canine osteoarthritis in the UK dog population and to investigate its associated behaviours. This will be carried out through the following objectives: 1) Highlighting the main risk factors associated with the development of OA and its predisposing conditions; (2) Calculating the prevalence, severity and duration of OA and the types of behaviours exhibited within the UK dog population; and 3) Investigating the current management of OA in primary care practice. Objective 1 will be covered in chapter 2 and objectives 2 and 3 in chapter 3, followed by a discussion which will include the findings from both studies.

# Chapter 2

## A Systematic Review and Meta-Analysis of Risk Factors Contributing to the Development of Canine Osteoarthritis and its Predisposing Conditions

## Abstract

Canine osteoarthritis (OA) is the chronic destruction and deterioration of articular cartilage surrounding synovial joints. It is commonly associated with pain and lameness in dogs, but the pathogenesis and risk factors leading to OA development are poorly described. The main aim of this study was to highlight the key risk factors contributing to the development of canine OA and its predisposing conditions. The scientific literature was systematically searched on Web of Science and PubMed following PRISMA (2009) guidelines, generating broad searches using pre-specified combinations of key words. Forty-four papers met the inclusion criteria and were evaluated and graded against set criteria. Data extracted from four full datasets provided were included in a fixed-effects meta-analysis for sex on OA, cruciate ligament disease and hip and elbow dysplasia. The meta-analysis results showed females had greatest odds of developing cruciate ligament diseases (fixed effect odds (FE) 1.715, 95% confidence intervals (CI) 1.31 to 2.24; random effect odds (RE) 1.600, 95% CI 1.10 to 2.33) and hip and elbow dysplasia (FE 1.173, 95% CI 0.978 to 1.407; RE 1.129, 95% CI 0.777 to 1.640), and that males have greatest odds of developing OA (FE 2.489 95% CI 1.253 to 4.943; RE 2.274 95% CI 0.707 to 7.309).. Whilst some risk factors may be unavoidable, such as sex, others can be prevented or managed, which may significantly decrease cases of OA in the dog population. This review provides a summary of the known risk factors associated with the development of OA and its predisposing conditions, identifying risks in the areas of genetics, (such as risk and protector genes) physiology, conformation (such as Norberg angle

and circumferential femoral head osteophytes) and environment and lifestyle (including age, sex and obesity).

## Introduction

Osteoarthritis (OA) is a common pain-causing condition that affects millions of people worldwide (Felson et al., 2000), as well as many species of non-human animals. It has been reported in a range of species from small laboratory rodents (Silverstein and Sokoloff, 1958), across companion animal species, to larger mammals such as horses (Neil et al., 2005). Osteoarthritis (OA) also termed degenerative joint disease, is so-named due to the chronic and progressive destruction and deterioration of the articular cartilage surrounding synovial joints, resulting in joint degeneration commonly associated with pain (Runge et al., 2008). Risk factors for development of OA stem from both systemic and local causes such as genetics, age, sex, obesity and previous injuries (strains/tears) (Felson et al., 2000). The aetiology of OA remains uncertain.

With over 8 million pet dogs owned in the UK (PFMA, 2016)[3], the threat of OA to dogs is considerable. Canine OA is a major problem worldwide for veterinarians, owners and breeders alike, with prevalence in North America said to range from 20% of adult dogs up to 80% of dogs over 8 years of age (Johnston, 1997). Prevalence estimates for OA in the UK dog population vary widely, from 6.6% of dogs of any age and breed attending primary care practices, (O'Neill et al., 2014) up to 20% of dogs >1 year of age (Clements et al., 2010). Duration of OA has not been extensively explored in the literature, however a longitudinal study has found that OA can potentially be a lifelong condition, occurring from younger through to geriatric years (Smith et al., 2006), with an early study finding the average age of dogs affected by shoulder OA was 10.2 years (Ljunggren and Olsson, 1975).

3 See: http://www.pfma.org.uk/pet-population-2016

OA is typically categorised into two types, primary and secondary. Primary OA is idiopathic, with potential causative factors remaining largely unknown, however degeneration in such cases has been associated with ageing in dogs (Clements et al., 2006). Secondary OA results from disease or insult such as cruciate ligament injuries, osteochondritis dissecans (OCD), patellar luxation, dysplastic conditions, or direct injury/trauma, which often occur before the geriatric years (Hegemann et al., 2002).

Cruciate ligament disease and rupture are common causes of pelvic limb lameness originating in the stifle joint in larger and giant breed dogs. Long-term degeneration caused by instability in the joint, can frequently lead to OA development (Taylor-Brown et al., 2015). Dysplasia typically occurs in the hip or elbow as a result of developmental malformation causing joint instability. This commonly leads to pain and lameness and often to laxity of the joint, causing further degeneration due to trauma (Worth et al., 2012). In many cases the pathogenesis of OA is said to have a genetic component, exacerbated through aspects of lifestyle, for example obesity (Smith et al., 2001).

Currently there is no curative treatment for OA; rather interventions aim to alleviate pain and slow progression (Kealy et al., 2000). Interventions include weight and nutritional management, symptom modifying drugs (such as non-steroidal anti-inflammatory drugs-NSAIDs, tramadol, and corticosteroids), and surgical intervention (Pettitt and German, 2015). Studies have shown that treatment with NSAIDs can significantly decrease the severity of pain associated with OA according to the Canine Brief Pain Inventory (Brown et al., 2008). Ultimately, preventative measures are the primary goal and further research is vital to deepen our understanding of the leading contributing factors to the development of OA.

To date, an in-depth scope and analysis of risk factors for OA and its predisposing conditions is lacking. This study aims to provide a comprehensive overview of all suggestive risk

factors that can be involved in the development of the most common forms of OA and its predisposing conditions, through systematic review and meta-analysis of published data. It is hypothesised that canine OA and its predisposing conditions will develop as a result of a combination of direct factors such as genetics that may be exacerbated by other factors related to the individual.

## Materials and Methods

### Literature Search

The peer-reviewed literature was systematically searched for papers which included factors that influenced the development of OA and predisposing conditions, using the approach outlined by the PRISMA (2009) guidelines (Fig 1). The online databases Web of Science (WoS) and PubMed were used to generate broad searches using key words within logical sequences (Table 1: See appendix). All identified papers from each search were stored in a Microsoft Excel database.

Literature searches were conducted during February and March 2016. Papers were initially sorted at Stage 1 by title, which had to include reference to dog/canine and OA or an associated disorder (listed in Table 1), with the implication that a risk factor was evaluated in the paper, with reference to words such as ‘prevalence’, ‘predictors’ or ‘susceptibility’. Stage 1 lists were independently evaluated by two reviewers, and inter-observer reliability calculated.

At Stage 2, included papers followed an abstract check for suitability according to the evaluation criteria. Papers that passed the inclusion criteria moved to Stage 3, where the full article was read (Fig 1). All papers across all stages were stored on Microsoft Excel

spreadsheets for each stage of the systematic search and included author names, year of publication, title, journal, issue, volume and page numbers.

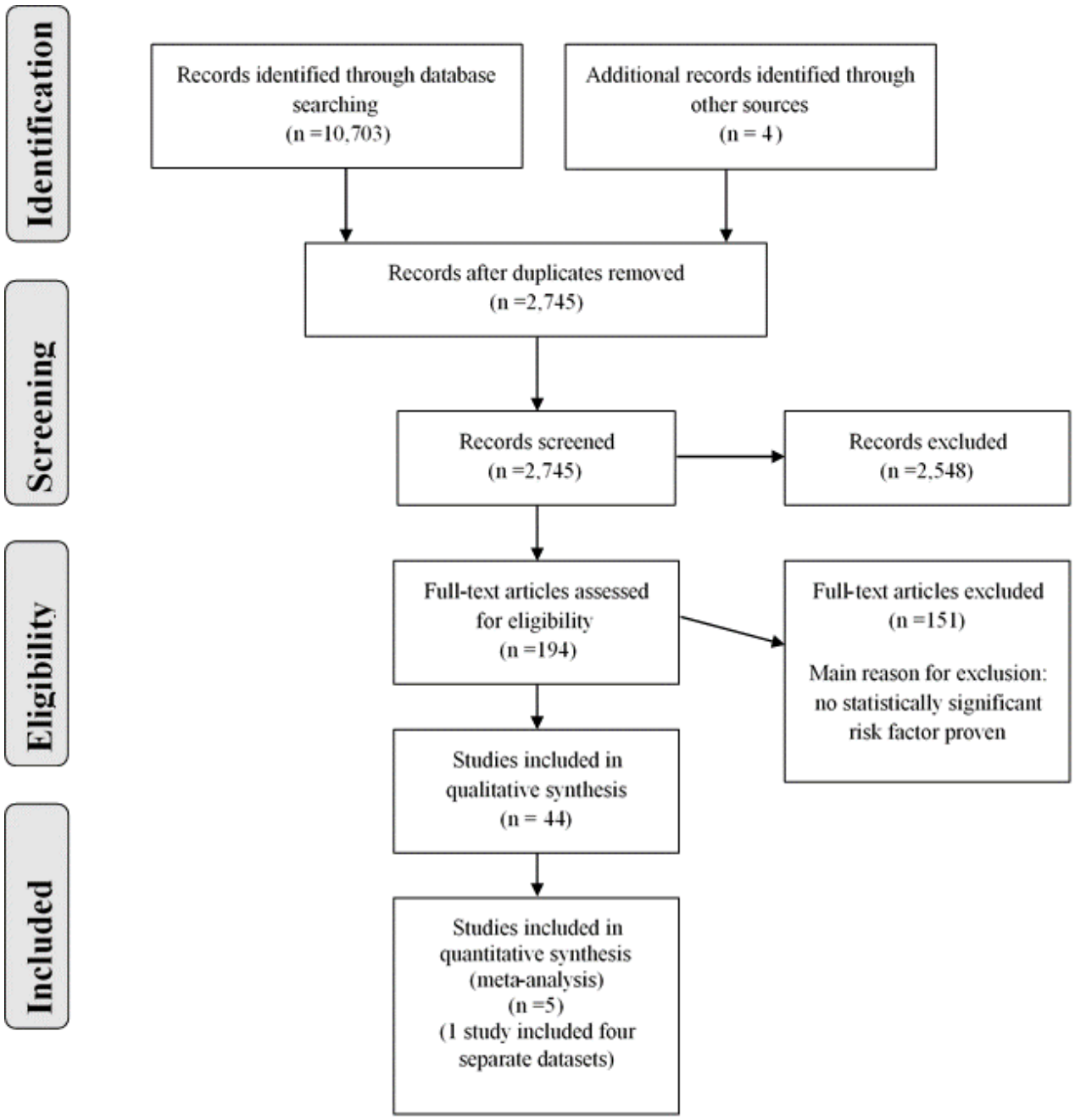


**Figure 1: Systematic Search Flowchart adapted from PRISMA Guidelines, 2009**

Finally, in Stage 4, additional papers were sourced from citations included in all Stage 3 papers. Following these searches the papers were grouped according to the condition they

were most relevant to and further divided into conformation, physiology, genetics and environment and lifestyle.

**Inclusion and Evaluation Criteria**

Peer-reviewed papers were included in the search with no timeframe filter implemented. Only papers either written in or translated into English were included in the search with no filters on country of origin of the literature.

The evaluation criteria included: peer reviewed papers in English on the topic of OA (excluding reviews), which provided statistically supported risks or demonstration of an increase in a dog's susceptibility to develop OA, such as (but not limited to) gene studies. Dogs included in the studies must have developed and been clinically diagnosed before or during the study or have radiographic evidence of early stage OA or one of its predisposing factors listed in the search terms. Studies could also include 'healthy' control cases.

**Study quality appraisal (QA)**

All of the included full text papers were subject to quality evaluation. The quality appraisal tool was created during this study based on recommendations from the Critical Appraisal Skills Program (CASP, UK) adapted to suit the variety of styles of studies identified during the literature search. The tool was adapted to assess study quality by evaluating methodological quality, (including biases) and outcomes/results of the studies to highlight the level of detail included within the paper (giving it a score of high: 7-10 [QA-H], medium: 4-6 [QA-M], or low: 0-3 [QA-L]) (Table 2: See appendix).

Finally, this was then combined in a Microsoft Excel spreadsheet along with title, authors and year, study design, statistical analysis used, results, the risk factors that the paper identified, overall sample (total number of dogs included in study) and control sample size (number of

control dogs) and whether power analysis was calculated and reported in the paper. The papers were grouped by individual disorder (See table 3).

### Statistical Analysis

A fixed effect meta-analysis using the Mantel-Haenszel method for calculating the weighted pooled odds ratio was performed using MedCalc for Windows, version 16.4.3 (MedCalc Software, Ostend, Belgium). Eighteen full datasets were requested by email from corresponding authors, for Stage 4 papers dated 2006-present. Four datasets were provided (one of which was split into 4) whilst the other 14 were not provided due to the author no longer having access to the dataset (n=3), the supplied addresses were no longer active and no other provided (n=3) and a lack of response (n=8). Only sufficient data was provided to enable the analysis of sex as a risk factor. The result of sex on the odds of developing three disorders (OA ($I^2$= 62%, 95% CI 0.0 to 91.3), Dysplasia ($I^2$=48%, 95% CI 0.0 to 84.8) and CCL disease ($I^2$=33%, 95% CI 0.0 to 97.8) were grouped onto forest plots and upper and lower confidence levels calculated.

## Results

WoS generated 2141 papers, PubMed generated 604, once duplications were removed. From the original search total, 432 paper titles were retained at Stage 1. At Stage 2, 194 abstracts were retained following the abstract check. In total, following stages 3 and 4, 44 papers met the inclusion and evaluation criteria for review (38 from WoS, 2 known to the authors, 1 from reference searches, 3 from the PubMed search. Note that 6 papers use the same data from a study on food restriction in a Labrador litter).

### Cruciate Ligament

There were 12 papers pertaining to risk factors involved in cruciate ligament disease and injury. Four papers were focussed on genetics (QA: 3H, 1M). Six papers were focussed on environment and lifestyle (QA: 6H). Two papers focussed on conformational risks (QA: 2H). Those as identified by the literature at greatest risk of developing cruciate diseases included: females (Whitehair et al., 1993; Adams et al., 2011; Taylor-Brown et al., 2015) (except bilateral rupture where males are more at risk (Grierson et al., 2011)) shown in the meta-analysis (Fig 2a), neutered individuals (Whitehair et al., 1993; Clements et al., 2008; Duval et al., 2009; Adams et al., 2011; Taylor-Brown et al., 2015), breeds inclusive of but not limited to Rottweiler, Golden Retriever and Labrador Retriever (Grierson et al., 2011), and overweight/obese individuals (Whitehair et al., 1993; Grierson et al., 2011). Identification of genes and chromosomes associated with cruciate ligament disease were also highlighted (Clements et al., 2008; Wilke et al., 2009; Baird et al., 2014a; Baird et al., 2014b). Age was often a conflicting finding, with some studies suggesting higher risk in younger dogs, aged 1-4 (Inauen et al., 2009), whilst others found older dogs >8 years (Taylor-Brown et al., 2015) to be more at risk.

**Dysplasia**

There were 16 papers in total associated with either hip or elbow dysplasia. One paper focussed on conformational risk factors (QA: 1H). Twelve papers focussed on environment and lifestyle (QA: 10H,2M). Three papers examined the genetics risk factors involved (QA: 1H, 2M). Those at greatest risk of developing dysplasia as assessed by the papers included: neutered individuals (Witsberger et al., 2008; Torres de le Riva et al., 2013; Hart et al., 2014), individuals with: lower pelvic muscle mass (Cardinet et al., 1997), higher distraction index (Choi et al., 2008), greater weight (Priester and Mulvihill, 1972; Sallander et al., 2006) and non-restricted feeding (Kealy et al., 1992). Breeds experiencing high prevalence included

Mastiffs, Boxers, Italian Corso dog, Labrador and Golden retrievers (Lavrijsen et al., 2014b). Certain types of exercise, e.g. running after balls (Sallander et al., 2006), and particular risk and protector genes were also found (Clements et al., 2008; Lavrijsen et al., 2014a). There were some inconsistencies in results including month of birth, where all literature suggested being born in winter was a risk factor (Leppanen et al., 2000; Wood and Lakhani, 2003; Worth et al., 2012), though some also found being born in spring (Leppanen et al., 2000) or autumn (Worth et al., 2012) also increased the risk. Age was an inconsistent finding with papers varying in results with older dogs (>8 years) (Leppanen et al., 2000), 2months -1year or 1-4years (Witsberger et al., 2008) all quoted as risks among the literature. Males were often quoted in the literature as being at greatest risk (Beuing et al., 2000; Witsberger et al., 2008; Torres de le Riva et al., 2013; Hart et al., 2014), however other papers (Lavrijsen et al., 2014b) as well as our meta-analysis results showed that females had greater odds of developing dysplasia (Fig 2b).

**OCD**

In total, 2 papers were identified by the systematic search relating to risk factors for OCD; 1 genetic (QA: 1M) and 1 environment and lifestyle (QA: 1H). Risk factor findings in the OCD literature include: being male (Guthrie and Pidduck, 1990) and lifestyle factors such as drinking from well water (as opposed to city water), playing with other dogs' daily and high dietary calcium (Slater et al., 1992). For patellar luxation, the literature indicated small breeds and females as most at risk; however, prevalence in larger dogs was noted to be increasing (Bound et al., 2009).

**Patellar Luxation**

One paper was identified by the systematic search relating to environment and lifestyle risks (QA: 1H).

**Osteoarthritis**

Fourteen papers were identified for OA; 4 identifying risks pertaining to conformation (QA: 4H), 3 physiology (QA: 3H), 5 environment and lifestyle (QA: 5H) and 2 genetics (QA: 1H, 1M). The direct risks involved in developing OA are discussed fully below.

## Table 3: Literature evaluation for all disorders

| Study authors and date | Risk Factors | Level of Detail (QA) | Type of Study | Overall Sample Size | Control sample size | Sample Size Calculated ? |
|---|---|---|---|---|---|---|
| **Cruciate Ligament Literature Evaluation** | | | | | | |
| Adams et al., 2011 | Females<br>Neutered<br>Rottweiler breed<br>Obesity<br>Older dogs (median 8 years) | H | CC | 1368 | 1179 | N |
| Baird et al., 2014a | Collagen genes significantly associated | H | CC | 749 | 456 | N |
| Baird et al., 2014b | Associated regions on Chr 1, 3 & 33<br>Haplotype blocks on Chr 1 & 33<br>Association with SORCS2 gene | H | CC | 271 | 172 | N |
| Clements et al., 2008 | Neutered<br>COL5A1 and RPL13A upregulated in susceptible breeds<br>14 genes upregulated in rupture<br>2 genes down regulated in rupture | H | CC | 17 | 12 | N |
| Duval et al., 1999 | Large breeds (9 predisposed)<br>Neutered<br>Greater body weight | H | CC | 1005 | 804 | N |
| Grierson et al., 2011 | Rottweilers, golden & lab retrievers<br>Younger dogs (4.3 years)<br>Males<br>Overweight | H | CS | 511 | N/A | N |
| Inauen et al., 2009 | Lower tibial tuberosity width<br>Greater body weight<br>Larger proximal tibial tuberosity angle<br>Younger | H | CS | 219 | 73 | N |
| Morris and Lippowitz, 2001 | Larger tibial plateau angle | H | C | 87 | 31 | N |

| | | | | | | |
|---|---|---|---|---|---|---|
| Necas et al., 2000 | Breeds: Am. Staff terrier, Rottweiler, Chow chow, St Bernard, Bullmastiff, Brazilian Fila, Lab retriever, Am. Cocker, German shorthaired pointer, Boxer<br>Hyperextended pelvic stance | H | CS | 183 | N/A | N |
| Taylor-Brown et al., 2015 | Neutered<br>> 3 years<br>Rottweiler & West Highland Terrier<br>Increasing body weight<br>Females | H | CC | 2,828 | 1,875 | Y |
| Whitehair et al., 1993 | 7-10 years<br>Neutered<br>Females<br>Rottweiler, Newfoundlan, Staff terrier<br>Greater body weight | H | CC | 602,317 | 591,548 | N |
| Wilke et al., 2009 | 86 markers associated with CCLR traits<br>4 associated markers on chr 3, 5, 13 and 24 | M | CS | 90 | N/A | N |
| **Dysplasia Literature Evaluation** | | | | | | |
| Beuing et al., 2000 | Males<br>Heritability estimate 0.28 | H | CS | 2114 | N/A | N |
| Cardinet et al., 1997 | Lower Pelvic muscle mass index | H | C | 82 | N/A | N |
| Choi et al., 2008 | High distraction index<br>Greater weight<br>Dogs kept indoors through growth | M | CS | 87 | N/A | N |
| Clements et al., 2010 | 10 SNPs as risk (5) or protector (5) genes<br>8 haplotypes as risk (5) or protectors (3) | M | CC | 647 | 438 | N |

| | | | | | | |
|---|---|---|---|---|---|---|
| Kealy et al., 1992 | Non-limited feeding | H | C | 48 | N/A | N |
| Krontveit et al., 2012 | Born Autumn and Winter<br>Urban/ suburban home (breeder home)<br>exercise on soft ground, daily stair use | H | C | 501 | N/A | N |
| Lavrijsen et al., 2014b | Bullmastiff, Boxer and Italian corso dog most prevalent<br>Females | H | CS | 35,046 | N/A | N |
| Lavrijsen et al., 2014a | Associated regions on chr 1, 3, 5, 8, 11, 12, 13, 15, 19, 20 25, 28, 32, 34 and X chromosome | H | CC | 122 | NS | N |
| Leppanen et al., 2000 | Born September - January<br>Older dogs | H | CS | 10,335 | N/A | N |
| Priester and Mulvihill, 1972 | Large and Giant breeds | H | CS | 1,193 | N/A | N |
| Sallander et al., 2006 | Excersise by running after balls/sticks<br>High fat intake/ energy from fat<br>Overfeeding/ High body weight | M | CC | 292 | NS | N |
| Torres de la Riva et al., 2013 | Early neutered males | H | C | 1,518 | N/A | N |
| Witsberger et al., 2008 | Neutered males<br>2 months - 1 year and 1-4 years<br>Large and Giant breeds | H | CS | 1,243,681 | N/A | N |
| Wood and Lakhani, 2003 | Born November to June (winter & spring)<br>Hip scores significantly correlated to relatives | H | CS | 9,657 | N/A | N |
| Worth et al., 2012 | Born Winter or Spring | H | CS | 5722 | N/A | N |
| **Osteochondritis Dissecans Literature Evaluation** | | | | | | |
| Guthrie and Pidduck, | Males | M | CS | 46 | N/A | N |

| | | | | | | |
|---|---|---|---|---|---|---|
| 1990 | Multifactorial mode of inheritance<br>Higher heritability in males | | | | | |
| Slater et al., 1992 | Drinking well water<br>Playing with other dogs daily<br>Not fed specialty dry food<br>High dietary calcium | H | CC | 91 | 60 | N |
| **Patellar Luxation Literature Evaluation** | | | | | | |
| Bound et al., 2009 | Small breeds<br>Females<br>Larger breeds increasing | H | CS & CC | 155 | 42 | Y |
| **Osteoarthritis Literature Evaluation** | | | | | | |
| Andrysíková et al., 2012 | High levels of GAGs<br>Higher GAGs in obese dogs | H | CC | 36 | 5 | N |
| Grondalen and Lingaas, 1991 | Males<br>Dogs with at least one parent with OA | M | CS | 2,046 | N/A | N |
| Hays et al., 2007 | Males (increased hip score & risk of OA)<br>Additive inheritance | H | CS | 137 | N/A | N |
| Hegemann et al., 2002 | Synovial 5D4 and TIMP-1 increased (ACLR)<br>Higher serum 5D4 and 10 fold lower serum TIMP-1 levels (FPC)<br>Synovial 5D4 and TIMP-1 were upregulated in dogs (patellar luxation)<br>Synovial TIMP-1 increased in hip dysplasia | H | CC | 133 | 30 | N |
| Kealy et al., 1997 | Non restricted feeding<br>Greater norberg angle and early joint laxity | H | C | 48 | N/A | N |
| Kealy et al., 2000 | Higher body weight<br>Non restricted feeding | H | C | 48 | N/A | N |
| Maccoux et | IL-1b expression in synovial fluid | H | CC | 13 | 5 | N |

| | | | | | | |
|---|---|---|---|---|---|---|
| al., 2007 | and fat pad<br>IL-6 expression in synovial membrane<br>Control synovial membrane have higher level of IL-8 expression<br>IL-10 gene expression in synovial membrane | | | | | |
| Mayhew et al., 2002 | Caudolateral curvilinear osteophyte<br>Distraction index | H | CS | 25,968 | N/A | N |
| Powers et al., 2004 | Caudolateral curvilinear osteophyte<br>Non restricted feeding | H | C | 48 | N/A | N |
| Runge et al., 2008 | Non restricted feeding | H | C | 48 | N/A | N |
| Runge et al., 2010 | High Distraction index<br>Higher Weight<br>Older dogs | H | CS | 4349 | N/A | N |
| Smith et al., 2001 | High distraction index<br>Weight | H | CS | 15,742 | N/A | N |
| Smith et al., 2006 | Non restricted feeding | H | C | 48 | N/A | N |
| Szabo et al., 2007 | Circumferential femoral head osteophyte | H | C | 48 | N/A | N |

[a]Abbreviations- C- Cohort; CC- Case-control; CS: Cross Sectional; H- High; L- Low; M- Medium; N- No; N/A- Not Applicable; NS- Not Stated; Y- Yes

**Meta-analysis**

4 study datasets (1 of which split into 4) were sent upon request and 1 paper provided enough information within the published article to be included within the meta-analysis. The forest plots demonstrate that females had greatest odds of developing cruciate ligament diseases and dysplasia, and that males have greatest odds of developing OA (Fig 2a-c), supported by Table 4- 6.

**Table 4: Odds, Upper and Lower Confidence intervals, z and *P* value and Fixed and Random weight (%) for cruciate ligament disease meta-analysis**

| Study | Odds ratio | 95% CI | z | *P* | Weight (%) | |
|---|---|---|---|---|---|---|
| | | | | | Fixed | Random |
| **Adams et al., 2011** | 1.974 | 1.430 to 2.725 | | | 69.27 | 54.81 |
| **Torres de la Riva et al., 2013** | 1.047 | 0.540 to 2.032 | | | 16.42 | 23.77 |
| **Torres de la Riva et al., 2013** | 1.497 | 0.736 to 3.044 | | | 14.31 | 21.42 |
| **Total (fixed effects)** | 1.715 | 1.314 to 2.239 | 3.969 | <0.001 | 100.00 | 100.00 |
| **Total (random effects)** | 1.600 | 1.100 to 2.328 | 2.458 | 0.014 | 100.00 | 100.00 |

**Table 5: Odds, Upper and Lower Confidence intervals, z and *P* value and Fixed and Random weight (%) for dysplasia meta-analysis**

| Study | Odds ratio | 95% CI | z | *P* | Weight (%) | |
|---|---|---|---|---|---|---|
| | | | | | Fixed | Random |
| **Worth et al., 2012** | 1.215 | 0.995 to 1.485 | | | 83.20 | 55.42 |
| **Torres de la Riva et al., 2013** | 1.745 | 0.804 to 3.787 | | | 5.56 | 17.17 |
| **Torres de la Riva et al., 2013** | 0.741 | 0.430 to 1.279 | | | 11.23 | 27.41 |
| **Total (fixed effects)** | 1.173 | 0.978 to 1.407 | 1.721 | 0.085 | 100.00 | 100.00 |
| **Total (random effects)** | 1.129 | 0.777 to 1.640 | 0.638 | 0.523 | 100.00 | 100.00 |

**Table 6: Odds, Upper and Lower Confidence intervals, z and *P* value and Fixed and Random weight (%) for OA meta-analysis**

| Study | Odds ratio | 95% CI | z | *P* | Weight (%) | |
|---|---|---|---|---|---|---|
| | | | | | Fixed | Random |
| **Andrysikova et al., 2012** | 1.181 | 0.377 to 3.698 | | | 37.46 | 45.25 |
| **Hays et al., 2007** | 3.908 | 1.615 to 9.457 | | | 62.54 | 54.75 |
| **Total (fixed effects)** | 2.489 | 1.253 to 4.943 | 2.605 | 0.009 | 100.00 | 100.00 |
| **Total (random effects)** | 2.274 | 0.707 to 7.309 | 1.379 | 0.168 | 100.00 | 100.00 |

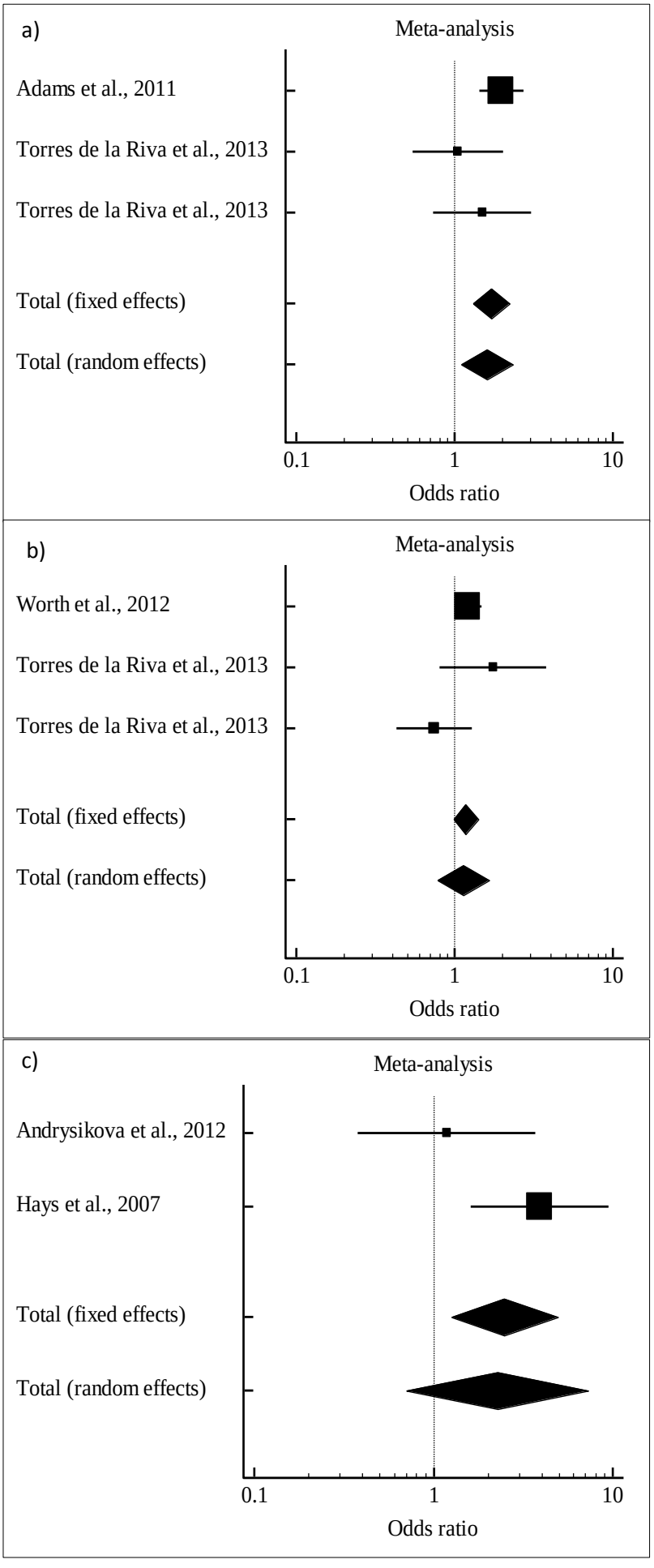


**Figure 2: Meta analysis showing: females have greatest odds for developing cruciate ligament diseases (a), females have greater odds for developing dysplasia (b) and males have greater odds for developing OA (c)**

## Discussion

OA occurs as a result of trauma, disease or insult as well as a combination of factors specific to OA. Conditions such as hip dysplasia, patellar luxation, osteochondritis dissecans, fragmented coronoid process and cruciate ligament disease can all be considered a risk factors for developing OA in dogs and therefore the risks for developing these conditions are also indirect risks for OA development. Better understanding these conditions will contribute to identifying 'at risk' individuals, in order to reduce and prevent the occurrence of OA in dogs. However, whilst these diseases and traumas remain a risk, there are additional identified direct risks for the most common forms of OA relating to genetics, conformation, physiology and environment and lifestyle.

Most cases of OA of the coxofemoral joint develops from hip dysplasia (Runge et al., 2010). Dogs with lower hip scores are significantly less likely to develop OA of the hip than those with higher scores (Hays et al., 2007), therefore this should be taken into account when selecting individuals for breeding (Wood et al., 2002). Both Norberg angle and distraction index have been significantly correlated with OA development. The distraction index is considered one of the greatest risk factors for OA, with the greater the score, the greater the risk. This is due to laxity in the joint resulting in damage and degradation often as a result of dysplasia (Kealy et al., 1997).

A genetic component has been recognised for OA. Offspring are significantly more likely to develop OA if one or both parents also had OA compared to offspring that did not have any parents with OA (Grondalen and Lingaas, 1991). Therefore, dogs diagnosed with OA or a predisposing condition, or first degree relatives (sire/dam, siblings, offspring) of that individual, should not be bred from as these conditions have been shown to be inherited. If

importing sires or dams, it is important to know full details of background and relatives to the individual.

Caudolateral curvilinear (CCO) and circumferential femoral head osteophytes can be used as early markers for predicting OA (Mayhew et al., 2002; Szabo et al., 2007), with a study showing that all dogs with a CCO were 3.7 times more likely to develop radiographic signs of OA than those without. Circumferential femoral head osteophytes have also been shown to be early markers of OA by Powers et al., (2004). Individuals with high hip scores should not be bred from, and dogs with early signs of OA such as CCO on radiographs should not be bred from either. Early detection of OA could prevent breeding from susceptible individuals, as many dogs will have been bred from before the condition was apparent. This will in turn reduce the number of offspring susceptible to OA, and therefore these early diagnostic tools as well as further research into susceptibility genes should be considered.

Additional diagnostic tools which may aid in early diagnosis include assessing the presence of cytokines and other biomarkers. The pathway that disrupts the balance of degradation and repair is said to be mediated by cytokines, and therefore measurements of these could indicate whether certain individuals are at risk of developing OA. Interleukins were found to be heavily involved, with significant increase in expression of various ILs in fat pads and synovial fluid and membranes of individuals with OA (Maccoux et al., 2007). Expression of these cytokines could therefore be used to identify individuals that may be at risk of developing or progressing to OA from other conditions.

Certain biomarkers have been identified in synovial fluid, membranes, urine and blood as early detectors of OA, which could aid diagnosis or prediction of OA. Glycosaminoglycan's (GAGs) have been shown to be involved in the degradation of cartilage and therefore can lead to the development of or accelerate the development of OA (Andrysíková et al., 2012).

A study has shown that increased levels of GAGs have been found in obese dogs, which most likely leads to the development of OA (Andrysíková et al., 2012). Other studies noted biomarkers such as synovial and serum 5D4 and TIMP-1 being either increased or decreased in conditions such as hip dysplasia or fragmented coronoid process (Hegemann et al., 2002).

Weight, age and sex are suggested as risks for developing OA. The literature suggests males having the greatest risk of developing OA as well as suffering greater severity. This was supported by the meta-analysis which showed that males had greater odds of developing OA than females (Fig 2c). This could be due to sex hormone differences as well as differences in weight between males and females (Hays et al., 2007). However, the outcome of developing OA because of sex can be significantly affected by other covariates such as neuter status and this needs to be taken into account when studying the effect of sex on OA development. A study conducted using paired littermates, one of which was on a control diet and the other on a restricted diet (25% less food than the control), showed that more dogs in the control group had an increased body weight and significantly increased development of OA, which was also more severe. The onset of OA was significantly delayed in the group with restricted intake. This therefore shows that a lean body condition and therefore improved phenotype should be maintained throughout the dog's life (Kealy et al., 1997). Despite the common association of OA with older dogs due to the natural progression of the disease and age related degeneration, a significant impact from diet was found from 1-5 years of age (Kealy et al., 1997). Restricted feeding has been shown to increase longevity of an animal which in turn could lead to age related degeneration and development of OA at an older age (Lawler et al., 2008; Runge et al., 2008).

OA and its predisposing conditions are frequently diagnosed in veterinary medicine demonstrating that they can have a large impact on canine welfare. As well as being

debilitating to the dog itself these conditions can have a large impact on owners too. High costs are associated with the treatment of these conditions – for example $1.32 billion spent on cruciate ligament ailments alone in the US in a year (Baird et al., 2014b). Additionally, OA is commonly seen in larger breeds which are often used as working or service dogs, which again negatively impacts owners of these dogs should they need to be retired from service prematurely.

The aim of this review was to collate all current information on the risk factors associated with developing OA and its predisposing conditions. The review showed that current literature, although fairly sparse, is mostly highly detailed in their descriptions of experimental method, and consistent across published results. This review highlighted clear gaps for further research in this area.

Further research to understand the pathogenesis of OA and its predisposing conditions would be advantageous and may improve the understanding of risk factors that lead to development of the diseases and further clarify identified risk factors in the existing literature. A deeper understanding of the risk factors contributing to cruciate ligament disease and rupture, dysplasia (for example the impact of exercise on its development), patellar luxation (for example explaining increased prevalence in large breed dogs) and OCD as well as the development of genetic screening tests, mapping of significant SNPs and gene regions, and identifying gene functions would be particularly timely. Prevalence data of OA resulting from predisposing conditions is currently lacking as is research into the rate of development from a predisposing condition to OA. Different risks also need to be further explored in order to highlight their relative effect on disease development and severity, for example obesity vs age. Finally, further exploration into early detection and diagnosis is needed in order to reduce the number of affected individuals that are bred from.

Although systematic reviews and meta-analysis are considered the top evidence reporting articles, there are certain to be some limitations. Author misinterpretation of studies and data is always a possibility, along with human error in the systematic search which may result in some literature being missed from the search. The evaluation of the studies is again, very subjective and occasionally opinions may bias/differ from others, which should be kept in mind. Limiting the criteria to include published only articles could lead to publication bias and result in unreliable or exaggerated results. Whilst the methodology of this paper is that of the systematic review as set out by PRISMA guidelines, overall it acts as a scope of risk factors contributing to the most common forms of OA. Due to the large variation in the studies and their data, this review is unable to determine or list definitive causes of specific types of OA due to limited studies that use controls.

In the case of this study, elbow and hip dysplasia's were grouped together. As two separate conditions this could lead to some limitations in the results, as this study provides a general scope of the risks that contribute to the most common forms of dysplasia, rather than the specific risks contributing to each specific disorder. Therefore, in future it would be beneficial to separate these as two conditions.

With regards to the meta-analysis, lack of data and absence of covariate variable data (e.g. neuter status when investigating effect of age on developing OA) could limit the outcomes of the study by affecting the results and the heterogeneity between datasets. Only a limited number of datasets were provided upon request and therefore study selection was limited and therefore may result in bias results. The heterogeneity of the datasets were all moderate according to the Cochrane Handbook, for Systematic Review Interventions (Version 5.1.0, 2011). Due to only a few responses to request for datasets, only 2 or 3 datasets were used in each meta-analysis which could explain the moderate heterogeneity between the datasets. The

OA analysis had the greatest heterogeneity likely due to the fact it had the fewest datasets and therefore lowest power. However, it has been argued previously that due to diversity of datasets included in many studies that heterogeneity is often unavoidable, and therefore shouldn't necessarily stop the analysis from being conducted (Higgins, 2003).

## Conclusion

To the authors' knowledge this is the first systematic review to produce a scope of risk factors for the most common forms of OA. This review provides a summary of published literature surrounding risk factors for OA and its predisposing conditions. OA is still too common within the dog population, and from the welfare and quality of life implications, prevalence reduction is important. Whilst some risk factors may be unavoidable such as neuter status (in preventing unwanted pets and reducing the risk of diseases such as mammary cancer) and age, others can be managed, particularly lifestyle factors for example keeping susceptible individuals lean. Identifying risks including genetics and breed type can lead to effectively implementing schemes to reduce prevalence through not breeding from individuals with the condition through better education of breeders. Additionally, better education of owners regarding breed selection and risk mitigation during ownership of their dog and finally improving advice and preventative treatment administered by vets will all increase dog welfare.

The disease still remains incompletely explained and therefore needs further investigation to allow for more prevention and treatment options to include cure rather than simply palliation. A positive finding of the review is the high quality of evidence in the papers selected for review as well as the fact that there were consistent findings across papers.

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# Chapter 3

**Epidemiology of Canine Osteoarthritis (OA) in the UK Dog Population as Assessed at Primary Veterinary Consultations**

## Abstract

In order to prioritise welfare-diminishing diseases in veterinary medicine, reliable information on prevalence, severity, duration and other aspects are crucial. Osteoarthritis (OA) is the most common joint disease in both human and veterinary medicine, posing a considerable challenge to canine welfare, and therefore epidemiological investigation in this disease is warranted. The aims of this study were to evaluate the epidemiology and impact of OA in dogs, and to describe clinical diagnosis and management of OA in primary-care veterinary practice. In order to investigate the psychological as well as physical impact of OA on quality of life, this study also aims to identify dog behaviours associated with OA. The VetCompass database was used to access clinical data from dogs attending primary-care veterinary practices in the UK. The study included all VetCompass dogs under veterinary care during 2013. Candidate OA cases were identified using a combination of search terms across the database and a random subset were then manually evaluated against a case definition. Of 455,557 study dogs, 16,437 candidate OA cases were identified of which 6104 were manually checked and 4196 were confirmed as OA cases. Additional data on demography, clinical signs and management were obtained then exported for analysis. The estimated prevalence (accounting for subsampling) of OA was 2.48% (95% confidence interval: 2.44-2.53). The mean age of diagnosis of OA was 8.6 years (± 3.6yrs, SD). Of the OA cases 19.9% had at least one behavioural complaint, with quietness and reluctance to exercise reported most frequently, whilst 88% of OA cases were given at least one treatment

for OA. Results of epidemiological findings will be discussed in relation to the impact on canine welfare, and how these metrics can be used to prioritise OA in veterinary medicine.

## Introduction

Osteoarthritis (OA) is the most commonly diagnosed joint disease in both human medicine and veterinary medicine (Mele, 2007). Osteoarthritis can be experienced as an extremely painful and sometimes debilitating condition (Pettitt and German, 2015). It is characterised by the progressive degeneration of synovial joints which leads to the development of reduced joint movement and lameness in dogs, as well as the presence of osteophytes and inappropriate new bone formations (Alam et al., 2011). The most frequently reported clinical and physical signs of OA in dogs include lameness, stiffness, reluctance to exercise and altered gait, all of which are suggestive of pain.

Veterinary treatments for OA at best alleviative symptoms, as there is no current curative treatment available, therefore the condition typically deteriorates over time (Pettitt and German, 2015). It is largely discussed as a multifactorial disease with a strong genetic component, exacerbated by aspects of lifestyle individual to each dog (Grondalen and Lingaas, 1991). OA occurs as a result of instability within the joint and is frequently associated with underlying conditions such as dysplasia, cruciate ligament rupture and osteochondritis dissecans, although it is not known what proportion of cases develop from these predisposing conditions (Rychel, 2010). The most common sites affected by OA include the stifles, hips and elbows. It is commonly considered a geriatric disease, although it can develop at any age; however, it is often only later in a dog's life that OA is seen to be a more significant problem and thus diagnosed when mobility is significantly affected following progressive degeneration (Rychel, 2010). It is suggested that >50% of cases are diagnosed in dogs aged 8-13 years (Mele, 2007). Other studies suggest age of onset depends

on breed and size, with average age of onset in Rottweilers estimated as 3.5 years, but an average of 9.5 years reported in smaller breeds (Mele, 2007).

Prevalence of OA is reported in the literature, but there are contradictions in the reports. Estimates have ranged from 6.6% from primary care data (O'Neill et al., 2014) to 20% (Pettitt and German, 2015) in the UK dog population. Estimates from North America report the prevalence to range from 20% in dogs >1 year, to 80% in dogs >8 years, of any breed (Johnston, 1997).

The duration of time a dog is affected by OA is not well discussed in the published literature. OA can occur at any age, however OA may not be clinically diagnosed until a later stage and may therefore be recorded as having a shorter duration than actually experienced by the individual (Rychel, 2010). Due to the difficulty of pinpointing the onset of the disease, duration studies are very difficult to conduct. Another difficultly when trying to determine duration arises as many cases develop from conditions such as hip or elbow dysplasia or cruciate ligament rupture. Although degeneration of the joint is likely occurring from before the diagnosis of the initiating cause, as the anatomical diagnosis is likely to be the one first noted, OA may not be considered to be present until much later in the disease course. Despite these difficulties, longitudinal studies have demonstrated that OA can potentially be a lifelong condition for some dogs (Smith et al., 2006), but further investigation is needed in this area to further highlight the proportion of cases that occur at different age categories to better understand the impact on welfare of this condition.

Measuring severity of diseases is complex and difficult. Previous literature has used severity scales in order to characterise, quantify and compare the severity of different canine conditions. Asher et al. (2009) proposed the Generic Illness Severity Index (GISID) using data collected from published literature, for scoring diseases based on prognosis, treatment,

associated complications and how the dog's behaviour has been impacted by the disease. Other studies use pain and behaviour scoring assessments through owner surveys in order to determine severity (Rialland et al., 2012); however, in the case of primary care data much of this is not explicitly recorded, and the complex nature of OA as a disease makes assessment of severity considerably harder. For this study, a novel calculation of severity was developed based on primary care data. This approach is based on a combination of proxy measures specifically suited to primary care data, which are designed to map onto the previously published GISID scoring system (Asher et al., 2009).

A broad range of pain associated behaviours have been discussed in the literature (Epstein et al., 2015), however little data exists regarding specific behaviours related to specific pain-causing conditions. Different individuals regulate chronic pain differently and can exhibit this in many ways such as through increased attachment to their owner, which may be considered a minor change in comparison to a change such as an increase in aggressive behaviour (Rutherford et al., 2012). It is the owner and veterinary professional's responsibility to recognise any behavioural changes that may be associated with chronic pain conditions. Psychological and behavioural aspects that are associated with pain are often overlooked in primary care, with the physical problem being the main focus (Roshier and McBride, 2012a&b). Therefore, behavioural manifestations of pain are likely to be under reported in primary care notes.

Under the Animal Welfare Act (2006), both physical and psychological aspects of a dog must be cared for (Section 4- Prevention of Harm). In the case of OA this means both the chronic pain and the associated behavioural manifestations need to be addressed. This highlights the importance of this investigation into the epidemiology, severity and behavioural aspects of OA due to the significant impact OA can have on canine welfare.

The aims of this study were (i) to calculate the prevalence, severity and duration of OA in the UK dog population from primary care data, and to identify if there are factors that affect severity score; (ii) to identify the risk factors for a diagnosis (in the case of this study, diagnosis refers to presumptive, radiographic or definitive diagnosis and excludes tentative or working diagnoses) of OA; (iii) to highlight how OA cases are clinically diagnosed and managed in practice; and (iv) to identify the most frequent behaviours associated with OA in order to investigate the psychological as well as physical impact of OA on quality of life. These aims will be answered using the following hypotheses: (i) prevalence of OA will be between 6 and 20% in the UK dog population; severity of OA will be affected by age, weight and breed differences and (ii) insurance status, age, sex, neuter status, and breed group are risks factors that increase the likelihood of an OA diagnosis. Aims (iii) and (iv) will be answered using descriptive analysis.

## Material and Methods

Ethical approval was granted by the College of Science's Ethics Committee at the University of Lincoln, UK in May 2016 (Reference number CoSREC125).

The study made use of data collected by The VetCompass Animal Surveillance project. This project collated de-identified Electronic Patient Record (EPR) data from primary-care veterinary practices in the UK for epidemiological research (O'Neill et al., 2014). Practices volunteered to participate in the project and to allow the recording of their clinical data within an appropriately configured practice management system. Information collected related to the owned dog population and included patient demographic (species, breed, date of birth, sex, neuter status, insurance status and weight) and clinical information. Practitioners recorded

summary diagnosis terms from an embedded VeNom Code[4] list (a standard set of clinical veterinary terms, used in referral veterinary hospital EPRs and first opinion veterinary practice management systems) during episodes of care as well as free-form text clinical notes, summary diagnosis terms, treatment and deceased status with relevant dates. EPR data were extracted from practice management systems using integrated clinical queries (Kearsley-Fleet et al., 2013) and uploaded to a secure VetCompass structured query language (SQL) database.

**Pilot Study**

Due to the large scale of the primary care dataset, initial pilot investigations were conducted. These were firstly run on the case definition which was decided after refinement using the information provided in the EPRs. A clear case definition was needed in order to reduce the number of false negatives and false positives, by excluding cases that were listed as differential diagnoses or other types of arthritis, such as auto-immune or septic. As many cases did not undergo imaging procedures, the case definition needed to be broadened to include other ways of determining OA cases, as a combination of signs and treatments.

Pilot tests were also run on the search terms used to find the cases within the denominator population. An initial list of search terms was drawn up including disease terminology, symptoms and treatments to identify the candidate cases. Terms were trialled multiple times and either kept or rejected based on their sensitivity and specificity. Terms were shortened and included the use of wildcards (e.g *) in order to allow for as many spelling variations and mistakes as possible. Search terms were refined to a point where at least 80% of cases returned by the search were true OA cases. This involved opening the cases returned by the search terms and identifying whether a diagnosis or strong evidence of OA was made either

[4] See: http://www.venomcoding.org/VeNom/Welcome.html

during or before (and continued through) 2013 according to the case definition. A total of 18 search terms were used in the final investigation. Search terms were also ran through the treatment notes using a variety of common OA treatments. These were again narrowed down to a smaller list to include those with highest sensitivity when searching through the EPRs for an OA diagnosis.

The study questions to be included on confirmed OA cases were also tested at the pilot stage to determine whether they were answerable using the given information within the EPRs and any that were not suitable were dropped from the full investigation. Using the study questions, data was recorded from the EPRs pertaining to; when and how the diagnosis was made, signs of disease, treatments, behaviour and death or end of EPR notes. Additional questions were included to allow for owner non-compliance with vet advice: e.g. 'was X recommended?', followed by 'was X implemented/prescribed?' (Table 7: See appendix). Certain questions were reviewed for the 3 months either side of the diagnostic episode of care (see table 7), to identify occurrences of relevance to the onset of OA. Changes or occurrences reported outside of the 3-month window were considered to have a lower likelihood of association.

**Main Study**

At stage 1, searches were conducted on the database to identify OA cases within a sampling time frame 1 Jan 2013-31 Dec 2013. Search terms used included: Osteoa*, OA, Degen* + Joint*, Joint dise*, DJD, Osteoph*, Arth*, and for treatment notes: Cartrophen ~ 2, Seraquin, Hill JD, Yumove, "Mobility treats", Cosequin, Green lipped (mussel), ArthriAid, Adequan, Specific canine cjd, joint support, Chondroitin. Osteoarthritis cases were included if the EPR showed evidence that the dog met the case definition during 2013. Cases were also included

if the records showed continuation of treatment or insurance claims from a pre-existing diagnosis before 2013.

An osteoarthritis case was defined as any dog with strong evidence for appendicular skeletal osteoarthritis recorded in the EPR (e.g. a final recorded diagnosis of or insurance claim for osteoarthritis (or synonym [see appendix])) or that was clinically managed for osteoarthritis e.g. rest, NSAIDs & supplements (or synonym [see appendix]) or where imaging findings were recorded that were indicative of OA (e.g. osteophytosis, enthesiopathy, new bone formation, subcondral sclerosis, Morgan's line).

Exclusion criteria as part of the case definition included:

i. Dogs where osteoarthritis, DJD or synonym was only listed as one of a differential list.
ii. Dogs with a diagnosis of osteoarthritis, DJD or synonym that was later revised to exclude osteoarthritis in the clinical notes.
iii. Dogs diagnosed with immune mediated, auto-immune, rheumatoid and septic arthritis/polyarthritis
iv. Dogs with a diagnosis of spinal conditions related to OA

At stage 2, EPRs were coded within the VetCompass database as a case or non-case, based on the EPR containing evidence matching the case definition. Every third identified case then underwent further data extraction using a series of study questions related to the patient, diagnosis, treatments and behaviour (Table 7).

At stage 3, relevant records were exported from the VetCompass database to a Microsoft Excel (2016) worksheet for data cleaning and analysis. Descriptive analysis was conducted within Excel for duration and behaviour observations. The prevalence estimate was

calculated from dogs that had OA during the study period (2013) either incident or pre-existing cases. Due to the timeframe of this project, the prevalence had to account for subsampling which meant prevalence was calculated from a subsample of the candidate population (37%) which was then used to calculate the prevalence of OA in the overall population. Prevalence was also calculated for the most frequently diagnosed breeds (number of OA cases in breed X / total number of breed X in sample population).

Three duration calculations were used to find an overall mean average figure for length of condition. Average duration was calculated using date of first diagnosis to date of final record, followed by date of first diagnosis to date of death (if occurred) and finally date of diagnosis to date of coding (for cases where death did not occur) as it was assumed it would still be currently present, even if managed. Percentage of life affected was then calculated using only individuals that died during the study period, using: duration (date of first diagnosis to death) / age at death.

**Severity Scale**

A severity scale was developed which combined a novel adaptation of the GISID severity scoring system (Asher et al., 2009 and Summers et al., 2010) and proxy measures related to OA, specifically designed for use with clinical data. Four areas of scoring included in the GISID score are prognosis, treatment, complications and behaviour. The areas scored from the sampled identified cases were adapted from the GISID, but had to incorporate suitable information available in the EPRs. The prognosis score was not applicable in the case of OA which is an incurable chronic disorder and therefore this was adapted to become signs of disease to reflect the level of pain an individual may be experiencing. The number of signs displayed by the dog such as limping, crepitus and stiffening could all be correlated with severity and the more signs shown the more severe the case is likely to be. Treatment was

included within the severity score and included all medical, surgical and lifestyle therapies. A score was awarded based on the number of treatments given to an individual the more treatment options provided by the vet the greater the severity is likely to be. The complications element of the GISID was adapted to become quality of life compromisers, due to the lack of complications noted within the EPRs. Quality of life (QoL) compromisers, such as restricted exercise, or weight management could have an impact upon the health and welfare of the individual and therefore affect QoL. Finally, behaviour was also included within this scoring system. However, in this system it was based upon 8 behaviours listed at the initial stages of the study and a score being awarded based on the number of behaviours exhibited by an individual. Behaviours chosen included aggression, reluctance to exercise and others associated with pain-related conditions.

A score was determined for each coded case based on point scale system (Signs and treatments both 1-6; QoL compromisers and behaviour both 1-4). (Fig 3). The minimum score obtainable was 0, whilst the maximum score obtainable was 20.

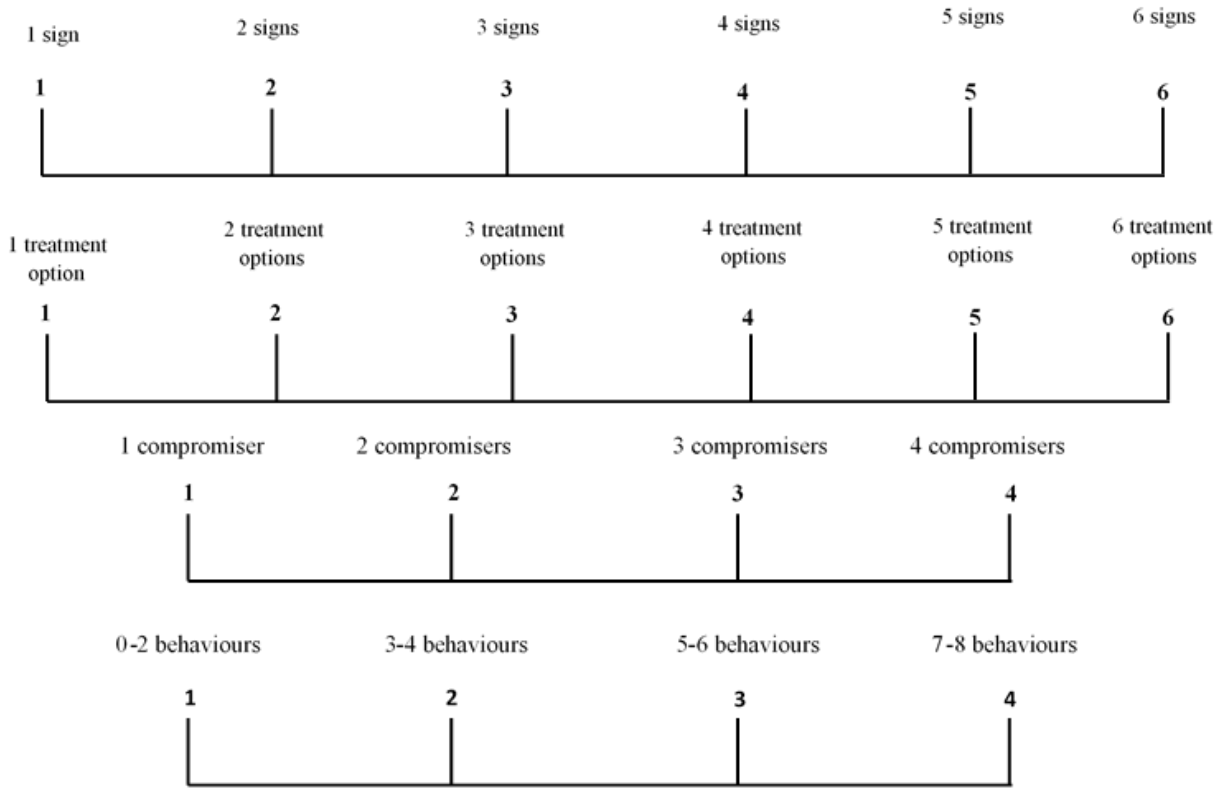


**Figure 3: Scale used to calculate severity using four areas of measurements from the EPRs**

## Statistical Analysis

The data showed normality when tested and therefore parametric modelling was used throughout the statistical analysis. A fully factorial univariate general linear model (GLM) ANOVA was run on the 1259 fully coded case individuals to test for an association between breed size (as determined by the UK Kennel Club breed standards[5]) and group (e.g. hound, terrier working, pastoral, gundog, utility or toy), age at diagnosis, duration of OA, whether weight loss was recommended, and severity score. Following this a multivariate GLM was conducted to test for associations between breed size, group, weight loss and age at diagnosis (independent variables), and duration and severity score (dependent variables), using SPSS v22.

[5] See: http://www.thekennelclub.org.uk/services/public/breed/

An unmatched case-control risk analysis was conducted on all cases (4197) (both incident and pre-existing confirmed cases) and non-case controls (controls defined as all dogs in the denominator population excluding unconfirmed cases from the candidate case list), using a binary logistic regression model to test the associations of breed type, sex, age, insurance, and neuter status with the development of osteoarthritis. Univariable models were run for each risk initially and statistically significant variables were then put into a multivariable model. An automated backwards elimination (Wald) model was used in order to remove the least significant variables from the final model (using the probability of the Wald statistic). Pairwise interactions were included for all variables in the multiple model, to explore potential interactions between terms not previously investigated. Biological relevance was considered for interactions before putting them in to the model. Finally, within Excel, behaviour observations were counted, and type of management of OA cases was also counted. An automated backwards elimination (Wald) binary logistic regression analysis was conducted on the 1259 fully coded cases to highlight the effect of breed size, age, insurance status and number of body sites affected on whether or not a dog was radiographed as a diagnostic method.

# Results

### Study Population

Overall, 455,557 dogs were included in the study as a denominator population, which had at least one EPR (not disease specific) either during 2013, or both before and after. Following the initial input of relevant search terms, 16,437 candidate osteoarthritis cases were identified from the denominator population (Table 8). Of these, 6102 (37%) were manually checked and 4196 of these were confirmed as osteoarthritis cases. 1259 (of the 4196 cases) underwent full data extraction using the questions listed in Table 7.

**Table 8: Table summarising the population characteristics of the denominator and candidate populations.**

| Population Characteristic | Denominator Population | | Candidate Population | |
|---|---|---|---|---|
| **Number of individuals** | 455,55 7 | | 16,437 | |
| **Average Age in 2013 (mean)** | 5.1 years | | 9.3 years | |
| **Sex** | Male: | 234,212 | Male: | 8,698 |
| | Female: | 219,033 | Female: | 7,715 |
| | Unknown: | 2,312 | Unknown: | 24 |
| **Insurance Status** | Insured: | 31,737 | Insured: | 2,981 |
| | Uninsured: | 26,029 | Uninsured: | 1,225 |
| | Unknown: | 397,791 | Unknown: | 12,232 |
| **Neuter Status** | Neutered: | 205,020 | Neutered: | 9,405 |
| | Entire: | 178,218 | Entire: | 3,266 |
| | Unknown: | 72,319 | Unknown: | 3,766 |
| **Purebred Status** | Purebred: | 340,769 | Purebred: | 12,579 |
| | Crossbred: | 98,931 | Crossbreed: | 3,568 |
| | Unknown: | 15,857 | Unknown: | 290 |

**Prevalence**

The estimate of prevalence of OA diagnosis in dogs attending UK primary-care practices overall was 2.5% (95% confidence interval: 2.44-2.53). In total, 163 breeds were diagnosed with OA. Breed prevalence was calculated for frequent breeds in the sampled cases and then using the denominator population for the most frequent breeds, in order to account for breed popularity. Frequent breeds were defined as those that had 50 or more individuals included in the OA diagnosed population (Table 9).

**Table 9: Number of cases in the most frequent breeds diagnosed with OA and the prevalence in sampled cases and overall**

| Breed | Number of OA cases | Prevalence in sampled in cases (%) | Number in overall denominator population | Breed prevalence overall (accounting for breed popularity in denominator population) (%) |
|---|---|---|---|---|
| **Labrador** | 753 | 17.9 | 23324 | 3.24 |
| **Staffordshire Bull terrier** | 248 | 5.9 | 21192 | 1.17 |
| **German Shepherd** | 224 | 5.3 | 8542 | 2.61 |
| **Border Collie** | 205 | 4.9 | 8584 | 2.39 |
| **Golden retriever** | 156 | 3.7 | 3807 | 4.10 |
| **Jack Russel** | 122 | 2.9 | 57943 | 0.21 |
| **West Highland Terrier** | 113 | 2.7 | 8411 | 1.34 |
| **Rottweiler** | 107 | 2.6 | 3724 | 2.87 |
| **Cocker Spaniel** | 95 | 2.3 | 33236 | 0.29 |
| **Cavalier King Charles** | 91 | 2.2 | 7100 | 1.28 |
| **Springer Spaniel** | 70 | 1.7 | 4060 | 1.72 |
| **Yorkshire Terrier** | 70 | 1.7 | 10798 | 0.65 |
| **English Springer** | 67 | 1.6 | 3768 | 1.78 |
| **Boxer** | 67 | 1.6 | 4398 | 1.52 |

**Duration**

Average age at diagnosis of OA was 8.6 years (±3.6 years SD) (average age of dog population in 2013 was 5.1 years (± 4.0 years SD) (Fig 4), with age of diagnosis ranging from 0 to 19 years. The average duration was 2 years (±1.7yrs SD), however it ranged from 0-11 years. The average percentage of life affected by OA was calculated at 11%.

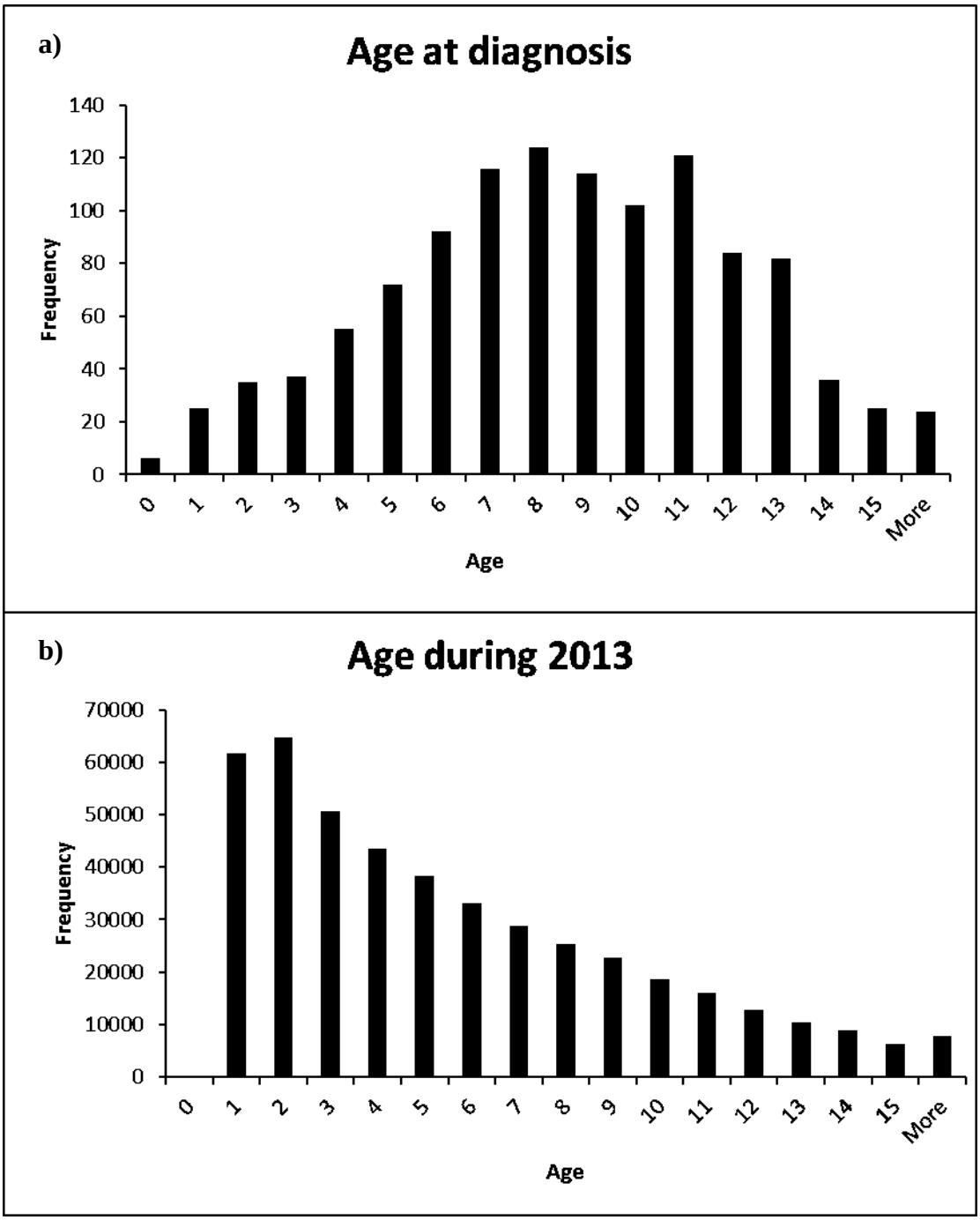


**Figure 4: a) Histogram showing age at diagnosis b) Histogram showing age of denominator population during 2013**

**Severity**

The average severity score for the sample of 1261 cases was 6.0 (±2.3 SD) with a range of 0-13 (out of a maximum 20). In the univariate model (dependent variable= severity), whether a dog was recommended to undergo weight loss had a significant association with severity score (Univariate ANOVA: F=16.4, p<0.001, df=1), with overweight individuals (weight loss recommended) having higher severity scores. Duration of disease also significantly affected the severity score (Univariate ANOVA: F= 5.6, p=0.018, df=1). Breed size, breed group and age at diagnosis, had no significant effect on severity score (Table 10). In the multivariate model (dependent variables = severity and duration) that tested for associations between breed size, breed group, age at diagnosis and whether weight loss was recommended, only whether weight loss was recommended was significantly associated with severity score (General Linear Model: F=15.4 p<0.001, df=1) (Table 11). During the period of study, 410 dogs died, of which OA contributed to the euthanasia of 264 dogs (64%)..

**Table 10: Results of Univariate ANOVA for association of variables on severity**

| Independent Variable | Dependent Variable | df | F | Significance |
|---|---|---|---|---|
| Age at diagnosis | Severity | 1 | .013 | .909 |
| Breed Size | Severity | 2 | 1.580 | .287 |
| Breed Group | Severity | 8 | .8.25 | .581 |
| Weight Loss recommended | Severity | 1 | 16.407 | .000 |
| Duration | Severity | 1 | 5.607 | .018 |

**Table 11: Results of multivariate general linear model for association of variables on severity score and duration**

| Independent variable | Dependent Variable | df | F | Significance |
|---|---|---|---|---|
| Age at diagnosis | Severity Score | 1 | .000 | .991 |
| | Duration | 1 | 2.149 | .143 |
| Breed Size | Severity Score | 2 | 1.515 | .221 |
| | Duration | 2 | .300 | .741 |

| | | | | |
|---|---|---|---|---|
| Breed Group | Severity Score | 8 | .801 | .601 |
| | Duration | 8 | 1.248 | .268 |
| Weight loss recommended | Severity Score | 1 | 15.401 | .000 |
| | Duration | 1 | 1.954 | .163 |

**Risk Analysis**

In the univariable binary logistic regression all variables (insurance status, age, sex, neuter status and breed group) were significantly associated with a diagnosis of OA (<0.10) (Table 12) and were subsequently included in the multivariable binary logistic regression. The multivariable model showed that insurance status (Binary Logistic Regression: Wald=51.9, p<0.001, df=1), and age (Binary Logistic Regression: Wald=381.1, p<0.001, df=1) were both significantly associated with an OA diagnosis where insured individuals were 2.2 times (OR 95% CI 1.8 to 2.7) more likely to have a diagnosis of OA than non-insured individuals. The breed groups that had statistically significantly decreased odds of a diagnosis of OA when compared with crossbreeds were: Gundogs, pastoral, toy, utility and working breed groups (Table 13). Sex and neuter status were insignificant in the risk analysis and therefore eliminated in the final model (Table 14). The final model had $R^2$ (Cox and Snell) of 0.027.

**Table 12: Results of univariable binary logistic regressions for analysis of risks contributing to an OA diagnosis**

| Independent Variable | Dependent Variable | df | Wald | Significance |
|---|---|---|---|---|
| Age at diagnosis | OA Diagnosis | 1 | 5892.059 | .000 |
| Insurance status | OA Diagnosis | 1 | 91.606 | .000 |
| Breed Group | OA Diagnosis | 7 | 1040.548 | .000 |
| Neuter status | OA Diagnosis | 1 | 633.959 | .000 |
| Sex | OA Diagnosis | 1 | 9.075 | .003 |

**Table 13: Results of binary logistic regression for association of breed group on having a diagnosis of OA compared to crossbreeds**

| Independent Variable | Dependent Variable | df | Wald | Significance | Odds Ratio |
|---|---|---|---|---|---|
| Gundog | OA Diagnosis | 1 | 14.982 | .000 | .420 |
| Hound | OA Diagnosis | 1 | .094 | .759 | .936 |
| Pastoral | OA Diagnosis | 1 | 13.728 | .000 | .220 |
| Terrier | OA Diagnosis | 1 | .018 | .893 | .968 |
| Toy | OA Diagnosis | 1 | 15.722 | .000 | .367 |
| Utility | OA Diagnosis | 1 | 24.092 | .000 | .232 |
| Working | OA Diagnosis | 1 | 16.572 | .000 | .292 |

**Table 14: Results of binary logistic regression for association between neuter status and sex and having a diagnosis of OA**

| Independent Variable | Dependent Variable | df | Wald | Significance |
|---|---|---|---|---|
| Neuter status | OA Diagnosis | 1 | .142 | .707 |
| Sex | OA Diagnosis | 1 | .763 | .382 |

**Behaviour**

Two hundred and fifty (19.9%) of the dogs with full data extraction had 1 or more behavioural issues reported in the EPR within ± 3 months of the OA diagnosis, with 342 separate behavioural issues noted. The most common behavioural issues included: (i) the dog is quieter (defined as lethargic, lack of appetite/thirst, not well in self less vocal and sleeping more) (24% of reported issues); (ii) alteration in normal behaviour (excessive licking/chewing, panting, clingier, soiling in the house) (24% of reported issues); (iii) reluctance to exercise (19% of reported issues); (iv) aggression (11% of reported issues); and (v) increase in vocalisations (defined as yelping, whining, barking) (9% of reported issues) (Fig 5)

.

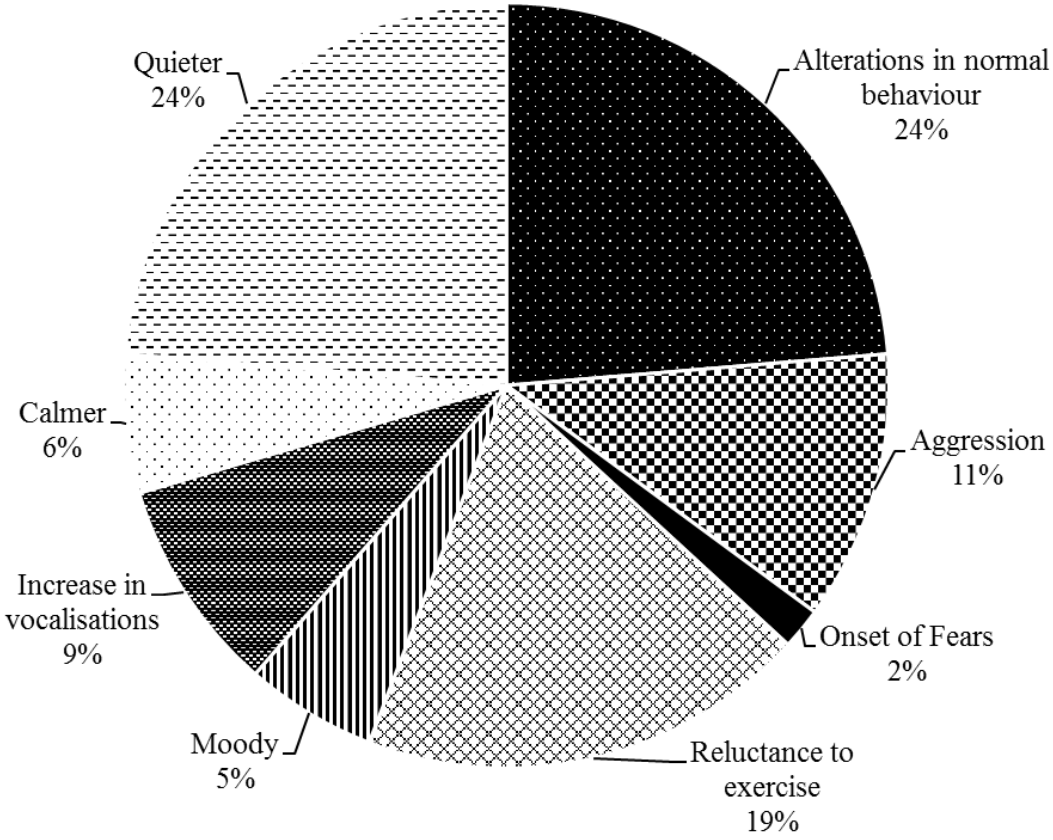


**Figure 5: Chart showing the percentage of behaviours exhibited by dogs recorded in the EPRs ± 3 months of OA diagnosis**

## Diagnosis and Clinical Management

A binary logistic regression test for independent variables (breed size, age, number of sites affected by OA and insurance status) affecting whether a case was radiographed or not was conducted. The model showed that breed size and number of sites affected had no effect on whether the individual was radiographed and were subsequently eliminated from the final model. Insurance status was statistically significantly associated with whether a dog was radiographed (Binary Logistic Regression: Wald=4.160, p=0.04, df=1) where insured individuals were 2.4 times (OR 95% CI 1.2 to 6.4) more likely to be radiographed than non-insured individuals. Age was also statistically significantly associated with whether a dog

was radiographed (Binary Logistic Regression: Wald=16.613, p<0.001, df=2), with the model showing young and adult dogs were less likely to be radiographed.

Eighty-eight percent of OA cases were managed with at least one treatment (i.e. medical or surgical treatments, excluded behavioural treatment) following the diagnosis of OA. 78% were treated using an analgesic drug, with NSAIDs being the most frequently used. 4.8% of cases were treated surgically (of these 4.8%, 79% were also treated with an analgesic), and 4.6% were referred for further investigation and/or treatments (of these 4.6%, 85% were also treated using an analgesic).

## Discussion

Prevalence estimates for osteoarthritis (OA) have ranged from 6.6% (O'Neill et al., 2014) to 20% (Johnston, 1997) and therefore there is a need for reliable and large scale prevalence data, in order to identify the impact of OA on canine welfare. In this study, prevalence was calculated at 2.5% from a sample population of 455,557 dogs attending primary care practices. The prevalence estimate of 2.5% is significantly lower than the previous estimates (O'Neill et al., 2014 and Pettitt and German, 2015). This is likely due to differences in methodologies (such as data type and sample sizes) and research populations (such as primary-care patients versus referral patients). However, the use of primary care data has been suggested to be more representative of the general dog population (O'Neill et al., 2016). It should be noted however, that due to the case definition designed to increase the specificity of the study, the prevalence estimate is likely to be slightly less than the true population prevalence rate, as cases that were likely to be OA had to be discarded due to lack of sufficient information provided in the EPR. The time frame of this study meant prevalence

had to account for subsampling and therefore there may be some variation with this figure estimate.

Additionally, the methodology of this current study using primary care data heavily relies on the input from the veterinarian treating the individual. As one vet's hip dysplasia may be another's OA due to differing examination and diagnostic procedures, there is likely some variation around the 2.5% estimate. Recent studies have shown significant variation between what is discussed in preventative medicine consultations such as annual booster appointments, versus specific health problem consultations. Preventative medicine consults provide a platform for the vet to detect other health problems such as OA that may be unnoticed by the owner, and therefore health discussions initiated by either the vet or the owner should be encouraged in these cases. However, this again relies on the veterinarian recording this in the EPRs (Robinson et al., 2016). A study examining the amount of the consultation that ends up recorded in the EPRs found that 64.4% of problems discussed during the consultations and 58.3% of actions undertaken were recorded in the EPR. Other variables that affected whether something was recorded within the EPRs included who raised the problem (i.e. owner or vet) and at what point it was raised during the consultation, and what action was taken. Ultimately it is the vet who decides what are the most important aspects of the consultation and what gets recorded in the EPR This therefore highlights some limitation to use of primary-care EPR data and demonstrates that some cases may be missed, or have reduced information due to lack of recording of data from consultations (Jones-Diette et al.). Many OA cases may also not have been included due to lack of follow up, or as OA was listed as one of a list of differential diagnoses. Also, cases progressing from previous conditions such as hip dysplasia or cruciate ligament rupture may not have been followed up in the notes as OA and therefore were discarded due to the specificity of the case definition

applied. However, irrespective, this estimate still equates to thousands of individuals affected by OA and therefore the problem still needs addressing.

The breeds with the highest prevalence are all breeds that have previously been associated with both predisposing conditions and OA. Additionally, there is the suggestion that larger breeds are more prone to developing OA, due to increased load on their joints **(**Grierson et al., 2011 and Lavrijsen et al., 2014b**)**. Therefore, the finding of frequent diagnosis in West Highland White Terriers and Cavalier King Charles Spaniels was interesting, as these are breeds that have not been frequently discussed as susceptible breeds for OA, however they have been suggested to be prone to patellar luxation (Bound et al., 2009). On another note, recent studies suggest obesity could affect up to 40% of dogs, and therefore this could explain why OA is being seen more in all types of breeds (Handl and Iben, 2012).

The mean age of diagnosis was 8.6 years, and the median age 9 years, showing diagnosis is often made in older individuals (Fig 4a). The age at diagnosis was quite old in comparison the overall population with the mean age as of 2013 when the EPRs were checked for OA, being 5.1years (±4.0 years SD) (Fig 4b). Therefore, either this is occurring more in older dogs and the associated degeneration the condition presents with is strongly correlated with age or it is only noticed later in life. The difficulty with OA as a disease is that it can present at any life stage, both during growth and in both adult and older dogs. In addition, OA can present differently symptomatically and on imaging and therefore may not necessarily be picked up by the owner or vet until it has developed to a certain level (Pettitt and German, 2015).

The range (19 years) for age at diagnosis showed that the minimum age of diagnosis was 0 years old. This shows that as OA can occur from a very young age and it can have long duration if these animals then live a long life. Many cases may well be diagnosed later in life,

but earlier signs may be missed and may only become apparent when the animal ages and therefore many more dogs could be suffering for a longer duration, with implications for welfare. In this study, the mean duration was 2 years, with calculations showing percentage of life affected as 11%. A study trialling OA treatment found an average duration of OA before starting the trial of 2.2 years demonstrating a similar figure to this study (Reymond et al., 2012).

Duration could be considered as a measurement of severity, the longer the duration the more severe the disorder is likely to be as there is increased time to suffer and progress. This study attempted to quantify severity based on proportion of life that is affected by what can be debilitating pain. Whilst other treatment studies acknowledge that OA has the potential for long term impact on health, there is very little information available on duration of OA itself.

The severity scale used was adapted from the current GISID scoring system (Asher et al., 2009) and proxy measures for severity, based upon the information provided about OA in the EPRs (Fig 3). This scale incorporated two measurements of severity from the dog and two from the perspective of the owner/vet in order to produce a score which is as valid as possible. The mean average score was 6, with a range of 0-13 (out of 20). Referring back to the GISID the range in this study would be equivalent to around 0- 11 on the GISID scale (based on differences between the maximum scores between these scales). Previous ranges found for similar conformational disorders include patellar luxation which had a range of 6-9, showing that on an individual basis, OA can be considered more severe. Other conditions that are frequent concerns to canine welfare that affect breathing and brain function include brachycephalic airway obstruction syndrome, (range 6-15), cranioschisis and syringomyelia (both 13-15). These are considered to be severe conditions with serious welfare impacts, and from this study the highest severity of score awarded for OA was within these ranges.

However, these scores are not directly comparable, and therefore severity scores between groups were calculated to identify if there are any differences in severity with certain variables.

Whether or not weight loss was recommended was a statistically significant factor in both the models, with dogs recommended to lose weight receiving higher severity scores. Dogs that are recommended to lose weight can be assumed to be overweight, therefore suggesting severity is correlated to excessive weight / obesity and therefore is highly important in OA management. Obesity is already well discussed as a risk factor for developing OA (Kealy et al., 1997, Kealy et al., 2000, Runge et al., 2010 and Smith et al., 2001) and this study suggests that it also contributes to the severity of the disease itself once developed. This is important to consider when managing OA, and any dogs that are overweight at diagnosis must have this brought to the attention of owners in order to alleviate some of the severity of OA for that individual. Breed size and breed group had no impact on severity. Age at diagnosis had no impact on severity score, however duration was significant for OA severity, suggesting that with progression of OA severity increases which is to be expected. Of the dogs reviewed in full, OA was a contributing factor in 64% of dogs euthanased. This is a high proportion and demonstrates that OA frequently contributed to death underlining its importance in veterinary medicine and dog welfare.

Insurance status was a significant 'risk factor' associated with whether a dog was diagnosed with OA, where insured individuals were 2.2 times more likely to have a diagnosis of OA than non-insured individuals. This has also been found in other studies relating to other diseases (Taylor-Brown et al., 2015). In the case of OA, it is likely that this finding is due to the need for specialist diagnostic images for diagnosis confirmation as well as the long-term nature of the condition and therefore treatment and costs. It may be the case that uninsured

individuals did not receive a firm diagnosis (i.e. the diagnosis was part of a differential diagnosis) and/or no follow up diagnosis in the EPRs due to the owner not bringing their dog back in, meaning they are excluded as cases from the study according to the inclusion criteria.

It is frequently mentioned that crossbreeds are healthier and less predisposed to developing diseases, particularly inherited disorders (Bellumori et al., 2013), however our results suggest that five breed groups (gundogs, pastoral, toy, utility and working breed groups) had significantly decreased odds of developing OA compared to cross breeds. This suggests there may be improvements in breeding practices or could be due to the fact that these breed groups may be prone to developing a variety of inherited disorders in comparison to crossbreeds and therefore OA may be overlooked in some of these cases where more severe disorders prevail. This again should be used and taken into account when choosing breeds and individuals to breed from.

Previous research has suggested that males have greater odds of developing OA than females (Hays et al., 2007) and that neutered individuals have higher odds of developing cruciate ligament problems and hip and elbow dysplasia (Adams et al., 2011, Taylor-Brown et al., 2015 and Witsberger et al., 2008). It was also highlighted in the meta-analysis in chapter 2, that males have greater odds of developing OA. In the current study, sex and neuter status were not statistically significant in the risk analysis. The study in this chapter used much larger datasets than many of the previous studies and the meta-analysis, as well as using primary-care data and therefore may account for the differences in results. Further studies on the effect of sex and neutering on development of OA would be beneficial.

The results from the current study highlight that age of diagnosis is most frequently dogs aged 8 years and over, supporting the studies that suggest it is more common in older dogs

(Runge et al., 2010). Many cases in younger individuals are likely developed from hip or elbow dysplasia and cruciate ligament rupture which have been shown to occur in younger individuals (Grierson et al., 2011, Inauen et al 2009 and Witsberger et al.,2008). In the case of this study, cases were only recorded at the point they were diagnosed firmly as OA and therefore could have occurred in much younger dogs from these conditions, but not noted as OA until much later on.

It has previously been reported that there is a lack of attention to behaviour within primary-care consultations and that the physical conditions are addressed more frequently than psychological complaints (Roshier and McBride, 2012a&b). One of the aims of this study was to investigate this further, and to identify behavioural issues that are commonly reported alongside OA. 19.6% of OA cases presented with at least one behavioural problem or change recorded with the EPR. This showed that behaviour was discussed in nearly a fifth of primary care consultations which, if followed up, may allow for better treatment of behavioural changes associated with pain-causing conditions. However, whilst this is a good improvement with respect to the amount of behavioural discussion in primary care (when compared to the studies previously mentioned), OA cases with behavioural complaints could be much higher than 19.6%, but not addressed in the EPRs. In addition, there is still a need for vets to diagnose behavioural changes and refer to behaviourists if appropriate, for treatment of these issues as this can otherwise contribute to decisions to euthanize. The most frequent behavioural complaints found to be associated with OA in this study included: quieter (defined as less vocal, lethargic, lack of appetite/thirst, not well in self and sleeping more), alteration in normal behaviour (e.g. clingier, excessive licking/chewing, panting, soiling in the house), reluctance to exercise, aggression and increase in vocalisations (defined as yelping, whining, barking) (Fig 5). This highlights the need to discuss behaviour within consultations when an individual appears to be presenting with pain, so that owners are more

likely to recognise pain-causing behaviours, and thus seek appropriate treatments. Also, making owners aware of the link between behaviour change and pain can enable them to notice subtle changes and bring their concerns to their vet earlier and thus allow for earlier diagnosis of OA.

In relation to clinical management of OA, 90% of cases were managed with at least one treatment following diagnosis, 80% of which included the use of an analgesic drug. 4.8% of cases were treated surgically, as well as 4.6%% being referred for further investigation and/or treatments. The low surgical intervention may be due to the risks relating to the surgery or the resulting implications on quality of life that can occur during rehabilitation and recovery. It could also suggest that veterinarians believe appropriate care can be administered without this type of intervention. Surgical intervention is usually seen as only necessary in the case of severe OA when other managements have been ineffective (Pettitt and German, 2015), as surgery results in further pain again, complications/risks and restricted exercise. The low referral rate could suggest that primary care clinicians believe that OA can be diagnosed and managed suitably in the primary care setting without the need for referral. Eighty percent of cases in this study were managed using an analgesic treatment, prescribed at the primary care consultations, the majority of these (97%) were NSAIDs. Whilst continual, long term use of NSAIDs has been suggested to sufficiently alleviate pain associated with OA, long duration of use can lead to complications and have an impact on quality of life through the development of organ problems, such as kidney or liver problems (Innes et al., 2010). In this study, 75% of cases were on treatment at the end of the record. This also highlighted that 20% of individuals were not treated using an analgesic treatment; this may be for a variety of reasons including the owner believing that their dog is not in pain. This indicates that there is a clear problem with vets convincing owners that their dogs are in pain when they present with signs such as limping and thus are in need of analgesia. This is a serious concern with

respect to animal welfare with many dogs unnecessarily suffering from potentially debilitating pain. This needs emphasising both in veterinary medicine and to owners in order to increase the awareness of signs of pain in dogs.

Exercise restriction was recommended in 21% of OA cases. It has been shown that osteoarthritis can significantly affect the gait of a dog, which in turn can impact unaffected joints and can therefore increase the severity of the disease for that individual. Exercise restriction is therefore important in order to prevent further damage to other joints until the pain associated can be managed for example by dietary management or by analgesic methods (Bockstahler et al., 2012). Exercise is recommended to be restricted but not stopped all together as this can be detrimental to the health of the dog (Petitt and German, 2015). For an active species however, exercise can be extremely important both physically and mentally (Taylor and Mills, 2007), so this finding suggests canine welfare sometimes is affected through treatment in the short term (e.g. where OA affects the biological need for exercise and activity as part of behaviour) in order to improve the welfare in the long term. Therefore, it could be suggested that restriction should only be recommended with severe disease, and the benefit of interventions to assist dogs to cope psychologically with restriction should be considered.

Twenty-eight percent of cases were recommended to undergo weight loss. This supports a correlation to being overweight and obesity on the development of OA. However, it could also suggest cases diagnosed with OA gain weight, perhaps through reduced exercise. This link therefore requires further investigation. Reducing food intake may again reduce the quality of life in the dog, a species that is well known for being food motivated. It has been shown in previous studies that diet alterations and food restrictions can have an effect on the behaviour and wellbeing of dogs (Bosch et al., 2007 and Crowell-Davis et al., 1995). This

demonstrates further that the management of OA can have a large impact on canine welfare and specific interventions must be carefully considered to ensure that they outweigh the implications of not implementing them.

At the start of the study it was acknowledged that radiographs may be required to provide a firm diagnosis of OA, however they do have their limitations (Pettitt and German, 2015). However, it was noted that many OA cases would not be accounted for if a radiograph had to be done to include them as a case. In some cases, radiographs were strongly recommended by the vet but rejected by the owner. Therefore, the case definition was expanded to allow for non-radiographed individuals to be included provided they meet other requirements of the case definition as these can't be discarded without potentially significantly under-estimating prevalence. A variety of reasons noted in the EPRs for not using radiography included lack of insurance or dogs age/other illnesses, and therefore a regression analysis was conducted to test for differences in insurance data, age, how many body sites were presenting with OA and breed type, in order to identify whether there were significant reasons for radiographing or not so as to acknowledge and understand why it may not be used as much.

Insurance status was a significant variable, where insured individuals were significantly more likely to be radiographed than non-insured individuals. This is no surprise as the cost of radiography was a clearly noted reason within the EPRs for not radiographing, and those with insurance are much more likely to be able to pay for radiographic diagnoses. This shows that a large proportion of uninsured individuals may suffer as a result of unaffordable treatment which is a concern for animal welfare. Age was a significant factor in whether a dog was radiographed, with the model showing young and adult dogs were less likely to be radiographed. This showed that older dogs were more likely to be radiographed despite the risks of anaesthetic and recovery being higher in older dogs. This study also showed that

duration affects severity and therefore older individuals may appear to present with more severe OA and thus be recommended for radiographs by the vet. This also supports that cases can't be discarded because they weren't radiographed as this would significantly underestimate the actual number of OA cases in further studies.

Whilst there is large potential in the analysis of large datasets such as this to better understand the welfare impact of a condition, there are a number of limitations. Firstly, only dogs that presented for consultations at veterinary practices were included in this study and consequently the results obtained could potentially not represent the entire population and for those that are not registered with a veterinary practice. Similar to this, animals registered with a vet and insured animals are a biased sample, as these owners are likely more invested in their animal than those that don't. This may result in a lower prevalence estimates as many other animals may have the condition but are not taken to the vet for diagnosis and management. Secondly, the data is only as good as the notes recorded during short consultations by the vet, as well as the level of information that is provided by the owner. This study relied on the vet to make diagnoses of OA, as well as record adequate data in the EPRs surrounding all aspects around the diagnosis. Therefore, there are possibilities that some dogs with OA were not diagnosed at all or that some recorded were also misdiagnosed. The denominator population include all dogs that attended a practice in 2013, whether presenting healthy (for preventative medicine consults) or sick (but not disease specific). Therefore, it may well be the case that undiagnosed cases exist in the denominator population too, or lack of data in the EPR meant they were not highlighted as candidate OA cases in this study. Again, in particular this could affect the reliability of the risk factor analysis. However, it should be noted, in the case of the risk analysis, unchecked candidate cases were removed from the denominator population.

The time frame of this study meant the methodology for calculating prevalence had to be account for subsampling, with only 37% of cases coded (as case or non-case) and therefore there may some variation with the overall figure estimate that was calculated for the population.

Finally, the severity score used in this study is again restricted to the information provided by the note taker on treatments and management or detail the owner at provides of any behavioural changes and signs. As this is, this study represents a pilot severity study using an OA specific scale. The current scores are stand-alone figures and not directly comparable to others. Further work in this area is recommended, to expand the current scale to be applicable to a range of primary-care disorders.

## Conclusion

This study found a prevalence estimate of 2.5% for OA in the UK dog population. Based on UK dog population estimates this equates to just over 200,000 individuals. It was also shown that diagnosis occurred in older individuals. This study supports that older dogs are diagnosed more frequently than younger dogs, however dogs as young as 1 year of age were diagnosed with OA during this study. The average severity score for OA in this study was 6/20, and both age and obesity were found to be significantly associated with severity. The average duration of OA was 2.2 years affecting 11% of life, suggesting OA poses a great threat to canine welfare and needs addressing in more depth in veterinary medicine.

Risk factors identified by this study include age, breed group and insurance status. Clinical management of OA was implemented in 90% of cases with use of analgesics being the most frequently used form of management. This is the first study known to look into behaviour reporting in primary care EPR and behaviours specifically related to OA. It was shown that

19.6% of OA cases presented with a behavioural complaint, also highlighting behaviours associated with OA, which suggests behaviour discussions are increasing in the primary care setting, but there is still room for this to improve. This highlights the need to discuss any behavioural complaints as well as physical signs as many pain related behaviours associated with OA were identified during this study.

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# Chapter 4

## Discussion

Osteoarthritis (OA) is a major health problem in dogs which warrants investigative epidemiological studies in order to improve canine health and welfare. Whilst OA has always been associated with ageing, (due to inevitable joint wear and degradation), it has become evident that OA can occur earlier in life in many cases and therefore has serious implications for dog welfare (Kealy et al., 1997). As a chronic and progressive disease, it is important to understand the aetiology and the risk factors that contribute to its development (Runge et al., 2008). Along with the aetiology and risk factors, it is important to calculate the prevalence, severity and duration of the disease in order to determine the overall welfare impact of the condition both at the individual and population level. This is therefore the basis of this epidemiological investigation, which set out to investigate epidemiological data on prevalence, severity, duration and risk factors, as well as highlight pain-related behaviours associated with OA and the level of behavioural discussion within primary care consultations.

### Risk Factors for Osteoarthritis and Predisposing Arthropathies

The initial aim was to conduct a systematic review on an epidemiological measure that has substantial literature, but remains largely unanswered. The gaps lay within risk factors and aetiology of OA, where previous literature did not provide the full picture. The current literature surrounding risk factors that contribute to developing OA, is sparse and often only features a single factor as the topic of discussion. Therefore, a comprehensive review of all current risks listed in the literature was chosen as the topic for review in this study- hypothesising that OA development is a result of a combination of factors. This was then broadened to include predisposing conditions, which could be considered risk factors. Many cases of OA develop from existing arthropathies, and also have risk factors. Four clear areas

of risks became evident from the literature search: genetics, environment and lifestyle (inclusive of signalment), physiology and conformation. To support the review element, a meta-analysis across the published literature was performed, to estimate the strength of evidence for an association between potential risk factors and OA.

The second study reported in this thesis was an epidemiological investigation into OA, which was conducted in collaboration with the VetCompass team at the Royal Veterinary College, London. The VetCompass project collects primary-care data from small animal veterinary practices around the UK. This dataset therefore provides an excellent source of information about a wide range of diseases affecting companion animal species in the UK, including canine OA. The aim of this study was (i) to estimate the prevalence of OA, (ii) to create a method of measuring severity of OA and to estimate the severity (iii) estimate the duration of OA. Risk analysis was also performed to support the previous literature review. Analysis was also conducted to identify key pain-related behaviours that are associated with OA, in order to provide education to allow for treatment of both physical and psychological elements, in pain-causing conditions. Prior literature has suggested that during primary care consultations behaviour is not discussed enough as consultations largely aim to provide relief for physical problems only (Roshier and McBride et al., 2013a&b). Therefore, this study also aimed to identify the frequency of discussions regarding behaviour within primary care settings.

Risk factors for the development of OA were highlighted in both the systematic review in chapter 1 and risk analysis during chapter 2. The key risks associated with developing OA highlighted by published literature suggested that joint laxity is the most common risk factor directly associated with OA development (Smith et al., 2001). When associated with hip OA, a key risk relates to the Norberg angle of the hip with the lower the angle the greater the risk of developing OA. A strong correlation to obesity and development of OA has been

suggested in the published literature due to higher weight results in more stress on joint, a finding that is common amongst other species. Whilst OA can be strongly correlated to obesity, non-weight bearing joints also develop OA as a result of other joint factors such as laxity and Norberg angle (Kealy et al., 1997).

Neutering is frequently mentioned as a risk factor and it is suggested that neutered individuals are at greatest risk of developing OA as a result of loss of gonadal protection hormones (Hart et al., 2014) and that males are more likely to develop OA. This was not borne out by the study reported in Chapter 3, see later.

Over exercising has been also shown as a risk due to the impact on the joints during developmental stages. Therefore, litters born in different seasons have demonstrated differences in susceptibility to developing OA. Litters born around autumn months were consistently shown to be less at risk of developing OA, likely due to reduced exercise levels outdoors during vital development ages (Worth et al., 2011).

Regarding predisposing arthropathies, large and giant breeds are strongly associated with developing conditions likely to predispose to OA, in particular cruciate ligament rupture. This is again likely due to extra stress on joints due to body size, similarly to OA where obesity is suggested as a risk factor (Adams et al., 2011). Genetics has also been implied as a main factor for development of OA (Necas et al., 2000). Congenital defects such as hip dysplasia frequently develop into OA and is said to do so as a result of both genetics and environmental stressors (Runge et al., 2010), as is patellar luxation (Bound et al., 2009).

The main findings in the literature suggest that OA is most strongly associated with genetics and obesity. For many of the predisposing arthopathies these are also considered risk factors, and therefore these should perhaps be the main targets in current practice to reduce cases of OA developing.

Genetics should be considered especially by breeders when selecting individuals to breed from and whilst many breeders likely do this, there are also likely many that do not. Given the finding in Study 2 that crossbreeds may be at higher risk for the development of OA, these considerations need to be taken beyond the pure breed breeders. Any individual or direct relative of an individual who has OA should not be bred from along with individuals with poor hip/elbow scores and joint laxity (Grondalen and Lingaas, 1991). Owners should also do appropriate research when sourcing a dog and should request health certificates for the dog where possible.

Studies show that osteophytes, biomarkers and cytokines can be used as predictors and prevention tools, as they are present as early signs OA (Andrysíková et al., 2012; Hegemann et al., 2002, Maccoux et al., 2007 and Mayhew et al., 2002). This should be further explored to better assist breeders in decision making before selecting breeding stock.

It can be concluded from the literature that OA is largely genetic disorder that is exacerbated through other stressors. Prospective cohort studies identifying the proportion of OA cases that develop from a particular risk factor, as well as determining the number of cases of OA that develop from other arthropathies would be beneficial to this area of study to further support the conclusions in this study and highlight any other particular risks.

The unmatched case-control risk analysis conducted during study 2, showed that insurance status and age were both significantly associated with the diagnosis of OA. Diagnosis of OA was shown to be in older dogs and therefore this study supports other studies suggesting that OA occurs more in older dogs (Smith et al., 2001). This is likely due to a combination of age related degeneration of joints and tissues, as well increased exposure to other stressors such as exercise, diet and injuries compared to younger dogs. However as previously mentioned this could also be a result of numerous things, such as the dog's ability to mask pain in the

earlier stages and only show signs when the disease progresses (Mathews et al., 2014), or the inability of the owner to recognise the dog is in pain and take it to the vet to obtain a diagnosis.

Often crossbreeds are thought to have hybrid vigour compared to their purebred parents as a result of reduced homozygosity. However, it was shown in this study that crossbreeds have an increased chance of developing OA, compared to certain purebred breed groups. This may also be due to the fact that the individuals that are bred are not checked and screened the same way purebred dogs are, for example the Kennel Club hip scoring program. This could result in those that aren't suitable for purebred registration to then be used in breeding crossbreeds, and thus resulting in poor genetics in the offspring, which end up increasing their susceptibility to disorders such as OA, instead of creating the desired hybrid vigour that crossbreeding sets out to achieve (O'Neill et al., 2013). This highlights again the need for screening individuals for all breeding purposes whether it be for purebreds or crossbreeds, particularly when using animals genetically prone to OA. There were 5 breed groups that had decreased odds when compared with crossbreeds for developing OA. This could suggest that any individual is susceptible and supports the fact although crossbreeds have been frequently considered 'healthier' than purebreds (Bellumori et al., 2013), this needs to be reconsidered in light of this study's findings and additionally the importance of environmental factors cannot be overlooked. A final possible explanation for this study's findings is that purebred dogs may have a number of inherited disorders where OA is overlooked by a more serious but simultaneous condition (Asher et al., 2009), whilst crossbreeds may develop just a single disorder such as OA, and therefore be more noticeable and thus diagnosed more in this case. Further investigations are required to determine the underlying causes for these observed differences and to determine the most appropriate explanation of this finding.

Whilst many studies suggest sex and neuter status as risk factors, in the risk analysis model in this study these variables were insignificant. Previous studies have used much smaller datasets than the one used in this study, which is likely to give a much better representation of the whole UK dog population. However, regarding neuter status, due to the nature of the methodology using primary-care data, the neuter status of the individual was its status at end of record rather than at the time of diagnosis of OA, and therefore could explain the difference in significance in this study compared to previous studies. It was hypothesised that insurance status, age, sex, neuter status, purebred status and breed group are risks factors that increase the likelihood of an OA diagnosis, which was partly accepted as insurance status, age, purebred status and breed group were all significantly associated with OA diagnosis, however sex and neuter status were not found to be significantly associated.

**Osteoarthritis Prevalence**

It was hypothesised that prevalence of OA would be between 6 and 20% in the UK dog population. A prevalence estimate calculated in this study was 2.5% showing that whilst many individuals suffer from OA, the hypothesis is rejected as this is much lower than previous estimates. Whilst this still equates to thousands of affected individuals, it should be taken into account that this is a conservative estimate and therefore the scale of the problem could be much greater. Even at the lowest estimate of 2.5% prevalence, OA is still of major concern- particularly in the case of the 20% that are not treated with analgesics, which is a major threat to canine welfare. There is very little prevalence data within published literature and there are many inconsistencies between estimates that do exist. O'Neill et al., (2014) calculated a prevalence estimate of 6.6% for OA. However, whilst this study similarly used primary care data, this was a broad study aiming to identify the top most frequently diagnosed disorders. This study differed from the current study in that no specific search

terms or case definitions were applied for accuracy of case versus non-cases differentiation. Instead an extraction of diagnosis term was made from EPRs, which could have led to an overestimate on prevalence, as it looked for the most frequently recorded conditions in practice without exclusion criteria for non-cases. However, what this study does show is that OA is an important disorder as it is included within the most frequently diagnosed disorders in veterinary practices.

Prevalence estimates were also made for popular breeds and in both the current study and O'Neill et al., (2014), popular breeds with the highest prevalence included Labrador retrievers, German Shepherds and Staffordshire bull terriers. O'Neill et al., (2014) also found that Border Collie and Jack Russell terriers were popular breeds with high prevalence, however in this current study, although they were found to be popular breeds, OA prevalence was not as high as previous estimates. As noted previously, this difference is likely due to the lack of specificity of the search terms and case definitions used in the earlier study, as it was conducted as a broad study to identify the most frequently diagnosed disorders, and therefore these other breeds may have been highlighted through the broad search but not defined as a case under a specific case definition.

Other prevalence estimates have been suggested to be as high as 20% prevalence in dogs over 1 year of age, however this is based on the North American dog population from 1997 (Johnston, 1997). The methodology of this study used radiographic diagnoses as cases, which is often thought of as the definitive diagnostic tool for diagnosing OA, due to the presence of new bone formations and abnormal appearances of the joint cartilage (Johnston, 1997). However, another study showed evidence of OA on radiographs doesn't correlate with clinical limb function of dogs with OA, which highlights the limitations of a radiographic diagnosis only study (Gordon et al., 2003). OA cases may be overestimated in this study due

to the appearance of the joint on the radiograph whilst clinical function of the joint may not actually be affected and therefore not progressed to OA. Equally however not all changes are shown on radiographs, and changes that are shown are not specific to OA so therefore this estimate of 20% should be taken with caution (Pettitt and German, 2015). On another note, the prevalence estimate study of 20% is frequently supported and quoted by insurance, nutrition and pharmaceutical companies which may have biased attitudes towards the results (Johnston et al., 2005). Many nutritional companies tailor prescription diets specifically for OA, with many pharmaceutical companies also producing many drugs used in the treatment of OA and so a high prevalence would be beneficial and increase custom to these companies. From the prevalence estimate (2.5%) in this current study it is expected that in the US $3billon a year (annual cost of $1,656 a year per animal) are spent on the management of OA, which in the UK would equate to around £200million a year (excluding cost of vet examinations and hospital stays) (Bartlett and Van Buren, 2009). This therefore shows the importance of this disorder to both the dog and owner highlighting the need for studies in this field.

The current study used both clinical symptomatic OA cases as well as radiographic cases due to the fact that radiographs were not used frequently and therefore would have considerably underestimated prevalence if relied on alone. This is likely a slightly low estimate due to the specificity of the case definition for the study, which meant cases that may well have been OA but were not recorded by the vet with the content required for this study were coded as non-cases. Further prevalence studies, particularly retrospective cohort longitudinal epidemiological studies, would be of benefit to the veterinary field in order to fully identify the extent of the disease within the UK dog population.

**Duration of Osteoarthritis**

Duration of a disease measures the length of time or percentage of life an individual is affected by a disease. With some diseases it is an easy measurement, however in the case of OA there is difficulty due to the nature of the disorder. As shown in this study, it can occur at any age and may go unnoticed until later stages when the dog begins showing signs. This is strongly influenced by both the animal and owner, as some individuals are able to mask pain more than others and equally some owners are more likely to notice changes to their pet than others. This study used a combination of calculations to calculate duration (2 years) and percentage of life affected (11%). This was supported by a previous study that found an average duration of 2.2 years (Reymond et al., 2012). This is a long time to suffer debilitating pain and therefore needs prioritising as a condition in veterinary medicine in order to maintain our duty to animal welfare. It was also shown that OA does not only occur in the end years of life and can range from 0 to 11 years in duration, which is a serious concern. This needs addressing and therefore requires future studies in preventing cases of OA for as long as possible in order to reduce its duration.

**Severity of Osteoarthritis**

Another aim of this study was to calculate the severity of OA for the patient. The scale used was adapted from previous severity/pain scales as well as proxy measures (Asher et al., 2009, Brown et al., 2009, Freeman et al., 2005 and Wiseman-Orr et al., 2006), specific to OA, with the aim in future to broaden the scale to be applicable to all disorders using primary care data. Four areas (described in Chapter 3) were used to comprise the scale. This included signs of disease, treatments, quality of life compromisers and behaviour. Signs of disease and behaviour are measures that are exhibited by the animal and therefore can be used to assess severity from a non-verbal patient through the way it presents the disease. These also rely on the owner recognising them and reporting them to the vet, and the vet recording them.

Treatment and compromisers to quality of life demonstrate the vet and owners' assessment of severity. As the observers of the patient, they implement management according to the perceived severity of the disease. Severity of OA was found to be greater in overweight individuals. This again highlights the importance of education of owners regarding the importance of lean dogs in order to reduce the severity of the disease as well as its development. The average severity score for the population is 6. With a range of 0 – 13 which shows there is a wide range in severity between individuals. As previously discussed in chapter 3, when compared with severe disorders such as syringomyelia and brachycephalic airway obstruction syndrome, the scores for OA fall with the equivalent ranges found by the GISID and therefore, the welfare effect of OA on an individual level can be severe and thus OA may need to be considered as a disorder of high priority, requiring appropriate management according to the individual severity (Asher et al., 2009). Despite a lower average score, OA can be of big concern particularly to frequently affected breeds.

The number of breeds found in this study to have at least 10 individuals affected was 38 (out of 156 breeds that had at least one OA case). It has been suggested that those disorders that have the greatest welfare impact have the highest severity and prevalence (Collins et al., 2011). OA can be considered to have moderate severity and prevalence across the entire UK dog population (which is likely to be underreported), affects many individual breeds, and is likely to have a large impact on canine welfare. It can therefore be considered as a serious concern to canine health.

It was hypothesised that severity of OA will be affected by age, weight and breed differences which was only partly accepted as severity was only significantly affected by weight (i.e. overweight individuals who were recommended weight loss), but not by breed group or size, or age.

## Behaviour

Pain-related behaviour has been previously discussed in the literature (Hansen, 2003) but the literature lacks data on behaviours relating to specific conditions. It has also been reported that behaviour isn't discussed frequently in a primary care setting (Roshier and McBride et al., 2013a&b). In this current study, 19% of cases had a behavioural change or problem mentioned within the EPR ±3 months from the diagnosis of OA. The actual figure for number of dogs with a behaviour problem may be much larger than 19% due to the fact that the methodology of this study relies on the owner mentioning behavioural elements during their primary care consultation. However, the top three behaviours found associated with OA were: quieter than usual, reluctant to exercise and alterations to normal behaviour (which involved toileting habits, eating and grooming) which are all absence of routine behaviours. Aggression, increase in vocalisations and moodiness were all also reported but less so; these are new behaviours that may occur at the onset of a stress trigger such as pain. This suggests that owners may be noticing more the changes to routine behaviour and not recognising so much new behaviours in their dog that are related to pain, or that many (but not all dogs) affected with OA pain respond with a particular behavioural profile. This shows that further education is required to owners about the onset of new behaviours that can occur with pain causing conditions, as well as to vets to be encouraged to ask about any changes/new behaviours in primary care consultations when a pain causing condition is diagnosed. This will enable the welfare of the animal to be maintained by treating both the physical and psychological element of the disease.

## Conclusion

This study has demonstrated the prevalence, severity, duration and behaviour of OA in the UK dog population. Not only does OA put a massive burden on welfare, but there is an

equally as large economic burden associated with the disease. The main risk findings from this study show that genetics are a main factor in the development of OA exacerbated through lifestyle and environment factors. However, the risk analysis during this study showed that crossbreeds are more at risk than certain breed groups and therefore heritability needs to be considered in terms wider than simply breed associated screening. The prevalence estimate shows that OA needs to be considered more of a priority in vet medicine due to the numbers of individuals affected by it. The chronic duration of OA affects welfare of the individual outlining the need for studies in prevention to reduce onset and percentage of life affected. Severity overall was shown to be moderate and strongly correlated with obesity, emphasising the need for better management of overweight dogs, and education to owners on the effect of obesity. Finally, this study showed that behaviours associated with OA include that the dogs are quieter than normal, reluctant to exercise and may also show more extreme behaviours such as aggression. It also showed that behavioural discussions do exist in the EPRs from primary care consultations but should continue and increase in order to treat both the physical and psychological signs of chronic pain conditions. This study can be used as a tool to educate owners of dogs with OA on types of behaviours to look out for and to vets the need to engage more in behavioural discussions during consultations.

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# Appendix

**Table 1: Search terms used for literature search (156 combinations in total)**

| Species | Disease | Key words |
|---|---|---|
| **Dog** | Degenerative joint Disease | Risk Factors |
| **Canine** | Osteoarth* | Predictors |
| | Dysplas* | Susceptibility |
| | Dislocat* | Cause |
| | Joint fracture | Prevalence |
| | Ununited anconeal process | Incidence |
| | luxat* | |
| | Cruciate ligament | |
| | Developmental elbow disease | |
| | Fragmented coronoid process | |
| | Osteochondrosis | |
| | Osteochondritis dissecans | |

**[a] Example search: Dog AND Dysplas* AND Risk Factors**

**Table 2: Paper Detail Evaluation Criteria**

| Area of Evaluation | Answer and Score Awarded | |
|---|---|---|
| | **Yes** | **No/Not Stated** |
| Is there a clear research question, aim or hypothesis and does the paper design suitably answer it with appropriate statistical analysis and results stated (values)? | 1 | 0 |
| Was the study period a suitable time frame? | 1 | 0 |
| Is the study design relevant to answer the study question? | 1 | 0 |
| Is the research applicable to the target population? | 1 | 0 |
| Are there any other explanations for the conclusions discussed? (e.g. other confounding variables, result variability due to methods) | 1 | 0 |
| Does the conclusion fit with other papers? | 1 | 0 |
| Does the study provide the full picture so that it is repeatable? | 1 | 0 |
| Was there use of controls? | 1 | 0 |
| Any bias in patient selection? | 0 | 1 (or Y but acknowledged) |
| Does the research hold any implications (either positive or negative)? | 1 | 0 |

**Table 7: Questions asked of the EPR data as part of data extraction**

**Patients:**
Is the dog an OA case?
**Problem Findings:**
Was osteoarthritis (or synonym) specifically recorded as a final diagnosis?
Incident or pre-existing in 2013?
Date of first diagnosis at any time in the clinical records
**Diagnosis**
Was the dog radiographed ± 3 months from the diagnostic episode of care?
Was there presence of osteophytes?
Did the dog have a CT ± 3 months from the diagnostic episode of care?
Single vs. multiple joints affected ± 3 months from the diagnostic episode of care?

**Presenting signs**
Was thickening of the joint (or synonym) recorded ± 3 months from the diagnostic episode of care?

Was the presence of crepitus (or synonym) recorded ± 3 months from the diagnostic episode of care?

Was limping/lameness recorded ± 3 months from the diagnostic episode of care?
Was stiffness/reduced range of movement (or synonym) in the effected joint/s recorded ± 3 months from the diagnostic episode of care?

**Behaviour**
Did the owner report changes in normal behaviours/addition of new behaviours ± 3 months from the diagnostic episode of care?
(Alterations in behaviour include soiling the house, panting, fidgeting, or generalised 'behaviour change' or 'acting up')
Did the owner report that the dog has become aggressive at home or out of the home (to people or other dogs) ± 3 months from the diagnostic episode of care?
Did the owner report the onset of fears (for example noise fear) ± 3 months from the diagnostic episode of care?
Did the owner report that the dog is reluctant to exercise ± 3 months from the diagnostic episode of care?
Did the owner report that the dog is moody ± 3 months from the diagnostic episode of care?
Did the owner report that the dog is quieter than before ± 3 months from the diagnostic episode of care?
(Quieter defined as less vocal, lethargic, slower or lack of appetite/thirst
Did the owner report any increase in vocalisations than before ± 3 months from the diagnostic episode of care?
(Vocalisations defined as howling, whining. Whimpering, yelping and barking)
Did the owner report that the dog is calmer than before ± 3 months from the diagnostic episode of care?
(Calmer defined as less playful, sleeping more or tires more easily)
**Treatment**
Was at least one veterinary treatment recommended for osteoarthritis at any time in the clinical records?

Was at least one veterinary treatment prescribed/administrated for osteoarthritis at any time in the clinical records?

(Veterinary treatment was defined as any pain relief, diet/weight management, supplement nutraceutical, hydro/physiotherapy, laser therapy or acupuncture used to manage the OA)

Was at least one analgesic agent recommended for osteoarthritis at any time in the clinical records?

Was at least one analgesic agent prescribed/administered for osteoarthritis at any time in the clinical records?

(Analgesia was defined as any corticosteroids, NSAIDS or Opioids)

What type of Analgesia type prescribed? (Glucocorticoid, NSAID, Opioid, or combination of these)
Was the analgesia prescribing/administration ± 3 months from the diagnostic episode of care??

Was there use of structure-modifying treatments for OA at any time in the clinical records? (E.g. cartrophen?)

Was weight loss/management recommended?
Was exercise restriction recommended?
Was surgical intervention/procedure recommended?

Was surgical intervention/procedure performed?

Was referral recommended for investigation/therapy?

Was referral undertaken for investigation/therapy?

Was the dog on treatment for OA at the final record of OA?

**Final Record information**

Date of final record overall

Single vs multiple joints affected at end of record for OA?

Did the dog die during the study?
Date of death
Method of death (euth/unassisted/unrecorded)
Did OA contribute to the death?

1) Allowed synonyms for osteoarthritis in EPR:

-OA/osteoarth
- Degenerative joint disease/DJD/Joint disease
-Arthrosis/Osteoarthrosis
-Arthritis (plus spelling variations)
- Degenerative arthritis
-osteophyte/osteophytosis
-spondylosis

2) Allowed synonyms for clinical management in EPR:

-NSAID (including: Meloxicam -metacam/meloxidyl, Carprofen- rimadyl, Previcox, Onsior)
-Strict rest/restrict exercise
-Weight loss/lose weight
-cartrophen/fen
-Tramadol
-prednisolone
-glucosamine
-chondroitin
-surgery/arthroplasty