New Zealand Veterinary Journal

ISSN: 0048-0169 (Print) 1176-0710 (Online) Journal homepage: https://www.tandfonline.com/loi/tnzv20

Canine hip dysplasia: phenotypic scoring and the role of estimated breeding value analysis

M Soo & AJ Worth

To cite this article: M Soo & AJ Worth (2015) Canine hip dysplasia: phenotypic scoring and the role of estimated breeding value analysis, New Zealand Veterinary Journal, 63:2, 69-78, DOI: 10.1080/00480169.2014.949893

To link to this article: https://doi.org/10.1080/00480169.2014.949893

Review Article

Canine hip dysplasia: phenotypic scoring and the role of estimated breeding value analysis

M Soo*† and AJ Worth*§

Abstract

Canine hip dysplasia (CHD) is a developmental orthopaedic disease of the coxofemoral joints with a multifactorial mode of inheritance. Multiple gene effects are influenced by environmental factors; therefore, it is unlikely that a simple genetic screening test with which to identify susceptible individuals will be developed in the near future. In the absence of feasible methods for objectively quantifying clinical CHD, radiographic techniques have been developed and widely used to identify dogs for breeding which are less affected by the disease. A hip-extended ventrodorsal view of the pelvis has been traditionally used to identify dogs with subluxation and/or osteoarthritis of the coxofemoral joints. More recently, there has been emphasis on the role of coxofemoral joint laxity as a determinant of CHD and methods have been developed to measure passive hip laxity. Though well-established worldwide, the effectiveness of traditional phenotypic scoring schemes in reducing the prevalence of CHD has been variable. The most successful implementation of traditional CHD scoring has occurred in countries or breeding colonies with mandatory scoring and open registries with access to pedigree records. Several commentators have recommended that for quantitative traits like CHD, selection of breeding stock should be based on estimated breeding values (EBV) rather than individual hip score/grade. The EBV is a reflection of the genetic superiority of an animal compared to its counterparts and is calculated from the phenotype of an individual and its relatives and their pedigree relationship. Selecting breeding stock on the basis of a dog's genetic merit, ideally based on a highly predictive phenotype, will confer the breeder with greater selection power, accelerate genetic improvement towards better hip conformation and thus more likely decrease the prevalence of CHD.

KEY WORDS: *Canine hip dysplasia, phenotypic scoring, estimated breeding values, genetic improvement, hip scores, hip laxity*

Introduction

Canine hip dysplasia (CHD) is a developmental condition primarily affecting medium-sized and large-breed dogs, which is characterised by instability of the hip joint, leading to degenerative arthritis (Todhunter and Lust 2003).

Canine hip dysplasia is a heritable and multifactorial disorder, meaning that its expression is influenced by the effect of several genes and many, often unidentified, environmental factors (Cook *et al.* 1996; Bliss *et al.* 2002; Smith *et al.* 2006). The disease is characterised by coxofemoral joint pain leading to lameness, stiffness and a progressive decline in function of the joint. CHD is one of the most common orthopaedic diseases affecting companion animals. Recognition of the heritable nature of the disease and use of effective breeding selection methods is critical to achieve a reduction in the prevalence of CHD. This paper will summarise the current understanding of the pathogenesis and radiographic diagnosis of CHD, and outline methods for selective breeding guided by genetic analyses.

Pathogenesis of CHD

Canine hip dysplasia was first described in 1937 as a congenital subluxation of the coxofemoral joint (Schnelle 1937). It is more correctly described as a developmental condition because the coxofemoral joints of dogs that later become dysplastic initially appear normal and congruent at birth (Riser 1975b). Whilst the original anatomical conformation of the coxofemoral joint and its surrounding structures are genetically pre-determined, continued growth and development are synchronised and dependent on mechanical function, joint congruency and the balance of forces applied across the joint. An alteration in any or all of these factors may affect or interfere with development of the hip joint (Riser 1975a; Frost 1989).

The hip joint is stabilised by its joint capsule and surrounding pelvic musculature. In 1966, Henricson, Norberg and Olson

* Massey University Veterinary Teaching Hospital, Institute of Veterinary, Animal and Biomedical Sciences, Massey University, Private Bag 11222, Palmerston North 4442, New Zealand
† Cahill Animal Hospital, Palmerston North, New Zealand
§ Author for correspondence. Email: a.j.worth@massey.ac.nz

http://dx.doi.org/10.1080/00480169.2014.949893

BVA	British Veterinary Association
CHD	Canine hip dysplasia
EBV	Estimated breeding value
FCI	Federation Cynologique Internationale
NZVA	New Zealand Veterinary Association
OFA	Orthopaedic Foundation for Animals
SNP	Single nucleotide polymorphisms

described a link between early joint laxity and the later development of CHD (Henricson *et al.* 1966). When laxity of the femoral head is present, the stabilising structures are assumed to fail to restrain the head of the femur within the acetabulum. The femoral head shifts laterally during weight-bearing, and force is concentrated on the dorsal acetabular rim. Prior to 6 months of age, the dorsal acetabular rim in dogs is largely cartilaginous and very plastic. Concentration of weight-bearing forces on the dorsolateral rim leads to microfractures and modelling of the acetabulum (Riser 1963, 1975b). The joint capsule is stretched and its attachments to the labrum can tear. After 6 months of age, changes in joint shape are only possible through the production or resorption of bone. Therefore, the phenotypic expression of CHD in genetically susceptible dogs may be preventable if coxofemoral joint congruency can be maintained until ossification of the acetabulum is complete (Riser 1975b).

The first 60 days of a puppy's life is thought to be the most critical period in terms of development of the coxofemoral joint, a period during which the joint is susceptible to modelling under abnormal stress loading (Riser 1975c). During this period, a puppy may be presented to a veterinarian because of pain from acetabular microfractures and traumatic synovitis. Clinical signs often improve with conservative management (weight reduction, confinement, analgesics) and many dogs become free of clinical signs until osteoarthritis develops and progresses to the stage of full-thickness cartilage loss later in life. In mild cases, the degree of laxity and change in loading is insufficient to induce osteochondral lesions that would result in lameness. In more severe cases, the trauma to the dorsal acetabulum caused by excessive loading leads to abrasion of the articular cartilage, inducing synovitis and effusion. Changes to the composition of the synovial fluid within the dysplastic hip joint reduce its ability to lubricate, leading to increased cartilage wear (Riser 1975c). As osteoarthritis progresses, joint effusion worsens the stability of the joint by loss of hydrostatic pressure (Smith *et al.* 1990). These changes further destabilise the joint, sometimes to the extent of coxofemoral subluxation or complete luxation (Riser 1975c).

Whilst the concept of laxity leading to subluxation is well accepted, the inciting cause of laxity is still uncertain. Factors that have been implicated in predisposing or causing a genetically susceptible individual to develop CHD include, but are not limited to: the disparity in the rate of maturity of the pelvic muscle mass and skeletal structures that support the coxofemoral joint in genetically susceptible dogs (Cardinet *et al.* 1997), spasms or contracture of the pectineus muscle (Ihemelandu *et al.* 1983), hormonal influence of relaxin and/or oestrogen (Steinetz *et al.* 2008), increased synovial fluid volume and osmolality (Lust *et al.* 1980; Kealy *et al.* 1993), caloric intake and rate of weight gain (Kealy *et al.* 1992; Comhaire and Snaps 2008) and level of exercise in the skeletally immature animal (Krontveit *et al.* 2012).

The genetic basis of CHD

Canine hip dysplasia has been accepted to be a heritable condition since the 1950s. Original hypotheses that a single gene with a recessive or dominant Mendelian pattern of transmission was responsible (Hutt 1967) were later doubted and the concept of incomplete manifestation and variable penetrance were promoted (Janutta and Distl 2006). By the 1970s, a multifactorial mode of inheritance was considered to be the most probable genetic basis for CHD (Leighton *et al.* 1977; Lust and Farrell 1977; Hedhammar *et al.* 1979).

In order to understand the concept of a multifactorial mode of inheritance, we must define the concepts of phenotype and genotype. The expression of a trait is known as the phenotype, which is the sum of the genetic and environmental effects, expressed as $P=G+E$, where P is the phenotypic value, G is the genotypic value and E is non-genetic, environmental deviation (Nicholas 2010a). An animal's genotypic value is the combined effect of the animal's genes at all loci affecting the phenotype of interest. For any measured trait, G is fixed at conception and E is the effect of all environmental factors influencing trait expression between conception and measurement of P. CHD may be expressed in a variety of phenotypes, each determined and measured by one or a combination of methods. For a quantitative trait, it is possible for two dogs of identical genotypes to express very different phenotypes under differing environmental influences. It is also possible that a genetically susceptible individual may have a hip phenotype that passes for normal, if environmental conditions are favourable. Multifactorial inheritance refers to inheritance of a phenotypic characteristic (trait) that is attributable to two or more genes with an unknown number of non-genetic (environmental) factors. In such multifactorial diseases, the actual number of genes determining the manifestation of the condition is commonly unknown. CHD is considered by many to be a quantitative trait due to its continuous phenotypic expression from normal to abnormal. Quantitative traits are determined by the action of different genes at many quantitative trait loci and the effects of each of the individual alleles are often not immediately distinguishable (Lust and Farrell 1977; Nicholas 2010a).

Several key steps have been taken to develop a genetic test for CHD (Zhu 2009). The canine genome has been mapped, opening the possibility that genes responsible for the expression of CHD may be identifiable (Guo *et al.* 2011). Mutations related to hip laxity and Norberg angles have been identified by mapping the chromosomes of cohorts of dysplastic Labrador Retrievers and disease-free Greyhound crossbred dogs (Todhunter *et al.* 2005). Twelve candidate (approximate chromosomal) locations for CHD were found. Further work on the German Shepherd dog genome using quantitative trait loci analysis revealed 19 candidate loci associated with CHD, located on nine different chromosomes, of which chromosome CFA9 was the strongest possible candidate (Marschall and Distl 2007). In another genome-wide association study, Pfahler and Distl (2012) identified three quantitative trait loci for CHD in Bernese Mountain dogs harbouring significantly associated single-nucleotide polymorphisms (SNP). Three SNP were found to be significantly associated with CHD on dog chromosomes CFA14 and 37, with candidate genes of interest being paraoxonase-2 (*PON2*) on CFA14 and fibronectin-1 (*FN1*) on CFA37. The *PON2* and *FN1* genes were hypothesised to be part of the pathogenesis of CHD due to their involvement with bone mineral density and extracellular matrix in cartilage respectively (Pfahler and Distl 2012). Four SNP associated with CHD and two SNP loci associated with hip osteoarthritis have also been identified in a separate study (Zhou *et al.* 2010). Friedenberg *et al.* (2011) identified an association between a mutation-deletion haplotype in the candidate gene, fibrillin-2 gene (*FBN2*) and CHD. The *FBN2* gene is the first gene reported to be associated with four phenotypic markers for the presence of CHD (the Norberg angle, distraction index, dorsolateral subulaxation score and the Orthopaedic Foundation for Animals (OFA) hip grade,

see later). Dogs homozygous for the deletion *FBN2* haplotype were found to have worse hip joint conformation (i.e. more severely affected by CHD) as characterised by having a lower Norberg angles value and dorsolateral subulaxation score, higher distraction index and poorer OFA hip grade. It was also found that dogs with incipient osteoarthritis at necropsy had an approximately 50% greater *FBN2* mRNA in their hip joint capsule in contrast to non-osteoarthritic dogs. However, the authors stressed that the *FBN2* locus did not explain all the genetic trait variation observed in CHD, indicating that other genes must contribute to the expression of the disease (Friedenberg *et al.* 2011).

Whilst current DNA marker technology is not yet sufficiently refined to be used in the selection of breeding animals, DNA marker information acquired via such means may be available to breeders in the future (Marschall and Distl 2007; Zhu *et al.* 2008; Zhou *et al.* 2010). It has been suggested that employing DNA markers as part of a genomic selection scheme would be an alternative means of reducing the prevalence of CHD (Sánchez-Molano *et al.* 2014). A genomic selection strategy involves a genomic (DNA) test that provides information on a large number of genotype markers in a population of phenotypically scored dogs. A subset of markers is then produced via linkage disequilibrium with the genes associated with the disease. These markers are later used to calculate genomic estimates of the true breeding values (genomic estimated breeding values), which are in turn used for subsequent breeding selections within the same breed. In the simulated study population, Sánchez-Molano *et al.* (2014) showed that genomic selection could have achieved greater genetic progress as compared to selection based on the phenotype alone (British Veterinary Association (BVA) hip scoring scheme). Compared to phenotypic selection, genomic selection accelerates the rate of genetic progress due to higher selection accuracy (Sánchez-Molano *et al.* 2014). Genomic selection also allows breeding selection to be carried out earlier because the DNA tests can be performed on animals at a younger age. More importantly, genomic estimated breeding values distinguish between littermates, thereby minimising the rate of inbreeding. Unlike phenotypic selection schemes, genomic selection removes environmental biases (such as age at scoring) which may artefactually influence breeding selection. Sánchez-Molano *et al.* (2014) emphasised that one potential drawback of this selection strategy is that due to the decay of the linkage disequilibrium between the genotype markers and causative loci, the accuracy of the genomic selection will likely decrease over time. Therefore, re-estimates (via phenotypic scoring) of the marker effects will still be necessary every few generations in order to maintain the level of accuracy. Until DNA marker technology has been further refined for routine use in screening for CHD, clinicians and breeders will have to rely on other modalities of breeding selection, as discussed in the following sections.

Phenotypic selection of dogs for breeding based on radiology: worldwide CHD scoring systems

Extended hip view

Due to the difficulty in objectively quantifying clinical CHD, radiological scoring/grading methods have been developed in an attempt to allow dog breeders to select less affected stock for breeding. There are several systems of radiographic screening currently in use around the world. The majority are based on images of the hips and pelvis taken under deep sedation or general anaesthesia, with the dog in ventral recumbency and with the hindlimbs extended (Flückiger 2007). An extended-hip view places the femoral head and neck consistently in a position which allows observation of the typical sites of coxofemoral joint osteophyte development. In addition, this view can reveal subluxation of the femoral head. However, the extent of subluxation can be underestimated due to the inherent positioning of the limbs for radiography and the level of sedation. If the patient is incompletely anaesthetised or sedated, it will respond to hindlimb extension by contracting its pelvic muscles, thereby improving the seating of the femoral head within the acetabulum and falsely lowering the extent of subluxation. Additionally, when the coxofemoral joints are positioned in the extended-hip view, the joint capsule and ligament of the head of the femur are both twisted, tightening the tensile elements of the joint capsule (Smith *et al.* 1990). As the tensile elements tighten, the femoral head is forced deeper into the acetabulum in a phenomenon known as "screw-home" tightening, a term borrowed from human medicine. In the canine hip, screw-home tightening may lead to false negative grades assigned to dogs screened at an early age, as osteoarthritis may not be evident on radiographs and the assessor is relying on the evidence for subluxation as an indicator of the severity of the disease. Furthermore, the extent of laxity seen on the extended-hip view is affected by the accuracy of patient positioning and the method of holding the limbs in extension. An oblique pelvic position increases the extent of femoral head coverage of one hip joint whilst lowering it on the other. If the dog's limbs are hand-held rather than being strapped in position for radiography, then the holder can also influence the degree of subluxation and falsely tighten the joints (Rendano and Ryan 1985).

Features of CHD on the extended-hip view vary depending on the age of the animal when it is radiographed and these features have been extensively documented by Riser (1975c). There is continual osteophyte development over the life of a dysplastic dog, indicating that osteoarthritis associated with CHD is progressive (Smith *et al.* 2006, 2012). Similarly, increased age at the time of assessment is significantly correlated with dysplastic radiological changes. These radiological signs are indirect markers of cartilage degeneration secondary to abnormal biomechanics of the hip joint. When CHD-affected patients were examined at the end of life, osteoarthritis was observed using histopathology in 96% (43/45) of the dogs compared to only 67% (32/48) of dogs seen radiographically (Smith *et al.* 2012). Therefore, osteophyte development observed radiographically is insensitive when compared to a gold standard of joint histopathology.

In the early stages of CHD, the radiological signs lag behind cartilage injury, but as a dog ages, radiography becomes more accurate at predicting the status of the hip joint morphology (Smith *et al.* 2012). When a dog is younger than 5 years of age, the radiological diagnosis of CHD is reliant on evidence of femoral head subluxation and/or osteoarthritis (Smith *et al.* 2012). In older dogs, radiological identification of CHD may encompass the presence of a shallow acetabulum, coxofemoral incongruity and osteoarthritis (Riser 1975c). After 6 years of age, newly diagnosed cases of CHD appear to be entirely dependent on radiographic evidence of coxofemoral osteoarthritis, with no new diagnoses based on subluxation (Smith *et al.* 2012).

The three most well-utilised CHD radiographic schemes are operated by the OFA in the United States of America, the BVA (United Kingdom and Australasia) and the Fédération Cynologique Internationale (FCI) in Europe (Flückiger 2007). A comparison of these grading schemes for CHD is shown in Table 1, but as each of these independent schemes is based on subjective assessments, direct comparisons between scheme grades are largely speculative. The OFA has been grading hip radiographs of dogs in North America and Canada for CHD since 1966, using subjective criteria (Flückiger 2007; Anonymous 2010). Dogs must be >24 months of age to be eligible for the scheme and an extended-hip view is taken under anaesthesia.

In Europe, the FCI is a cooperative of national kennel clubs which has been screening dogs for CHD for over 40 years (Flückiger 2007). Dogs must be >12 months of age or >18 months of age for the large and giant breeds. The FCI scoring system combines subjective assessment of the degree of subluxation, congruity of the femoral head and acetabulum and osteophyte development on the extended-hip view with objective measurement of subluxation using the Norberg angle (Morgan and Stephens 1985; Henry 1992). A normal Norberg angle is considered to be 105° and greater; however, this upper limit of normal value varies between breeds and should be interpreted with caution (Tomlinson and Johnson 2000; Culp *et al.* 2006). Additionally, the Norberg angle is affected by screw-home tightening, as described above. Analyses of inter-observer agreement of the FCI system showed that assessment of the morphological characteristics of the hip joints and the final score are highly variable between observers (Verhoeven *et al.* 2007, 2009).

In the United Kingdom, the BVA and the Kennel Club implemented a CHD screening programme in 1965. This technique of hip scoring was also adopted in Ireland, Australia and New Zealand (Flückiger 2007). Up to 53 demerit points are awarded *per hip* in nine categories to yield a total score of 0 (best) to 106 (worst) (Dennis 2012). Dogs are eligible for this programme from 12 months of age.

The New Zealand Veterinary Association (NVZA) introduced the Canine Hip Dysplasia Scheme in the mid-1980s (Hunter 1986) in co-operation with the New Zealand Kennel Club. A national computerised database was maintained from 1989. Dogs need to be >12 months of age to be eligible to be scored under this scheme and it is recommended that giant breeds are scored at 18 months of age or older. Readers are referred elsewhere for further information on the NZVA CHD scheme (Worth *et al.* 2009; Anonymous 2011).

Table 1. An attempted comparison of the different grading systems for canine hip dysplasia, modified from Verhoeven *et al.* (2012). Each system is based on subjective criteria such that direct comparisons are largely speculative, therefore, this table is only a guide.

	Grading System and Grade				
	Fédération Cynologique Internationale (Europe)		British Veterinary Association (UK)		Orthopedic Foundation for Animals (USA)
Descriptor					
No signs of hip dysplasia	A	NA[a] >105°	A1	0–4 (not >3/hip)	Excellent
			A2	5–10 (not >6/hip)	Good
Near normal hip joints	B	NA ≤105°	B1	11–18	Fair
			B2	19–25	Borderline
Mild hip dysplasia	C	NA 100°	C1	26–35	Mild
			C2		
Moderate hip dysplasia	D	NA 90–100°	D1	36–50	Moderate
			D2		
Severe hip dysplasia	E	NA <90°	E1	51–106	Severe
			E2		

[a] The Norberg angle (NA) measured under the Fédération Cynologique Internationale scheme allows for the objective assessment of femoral head subluxation. A normal NA is considered to be ≥105°.

Distraction view

Building on the link between early joint laxity and later development of CHD described by Henricson *et al.* (1966), the concept of passive versus functional hip laxity was introduced to distinguish between subluxation evident radiologically compared to subluxation induced during weight-bearing (Smith *et al.* 1990). Those authors proposed that the joint capsule, round ligament of the femoral head and the hydrostatic stability factor are passive constraints to hip laxity and each play a role in maintaining congruency between the femoral head and acetabulum. The active constraints are the muscles surrounding the hip joint capable of imparting a force that reduces the femoral head into the acetabulum. Passive constraints restrict the amount of hip extension possible as well as creating a force that acts to drive the femoral head into the acetabulum, minimising laxity. If the constraints maintained by the soft tissue surrounding the hip joint do not function properly, the coxofemoral joint will not receive and effectively transmit load during weight-bearing. The inability or failure of these soft tissue passive constraints to limit the amount of lateral displacement of the femoral head in the relaxed dog is defined as passive laxity. Functional laxity is defined as the lateral translation of the femoral head out of the acetabulum during weight-bearing. Passive laxity is a pre-requisite for, but not a cause of, functional laxity and may not always correlate with an equal extent of functional laxity (Smith *et al.* 1990). Passive laxity has been reported to be highly correlated with the development of osteoarthritis and the clinical signs of hip dysplasia (Smith *et al.* 1990, 1995). Smith *et al.* (1990) developed a stress-radiographic method (distraction radiography) using a radiolucent fulcrum placed between the femurs to quantify the degree of passive laxity in an anaesthetised or heavily sedated dog. The adjustable radiolucent fulcrum is placed between the thighs of the dog and the femurs are pulled together by gripping the distal limb, inducing femoral head subluxation at which point a radiograph (the distraction view) is taken (Figure 1). This distraction radiography method formed the foundation of PennHIP (formerly the University of Pennsylvania Hip Improvement Program), which became commercially available in 1993 (Anonymous 2013). The PennHIP distraction index is a measure of passive hip laxity and is calculated by determining the degree to which the femoral head subluxates relative to the acetabulum. The linear distance between the centre of the acetabulum and the centre of the femoral head on the distracted radiographic view is divided by the radius of the femoral head to achieve a unit-less measure of laxity; the distraction index (Figure 2). The PennHIP evaluation comprises three ventrodorsal radiographic views; the distraction, compression and extended-hip views. The extended-hip view is used to assess the presence or absence of osteoarthritis and the compression view is used to assess the overall coxofemoral congruency. The presence of osteophyte

Figure 1. Photograph showing positioning of a dog for measurement of the PennHIP distraction index. A radiograph is taken with the dog heavily sedated or anaesthetised and positioned in ventrodorsal recumbency with the distraction device placed between the thighs. The operator uses the device as a fulcrum to achieve distraction of the coxofemoral joints (passive hip laxity).

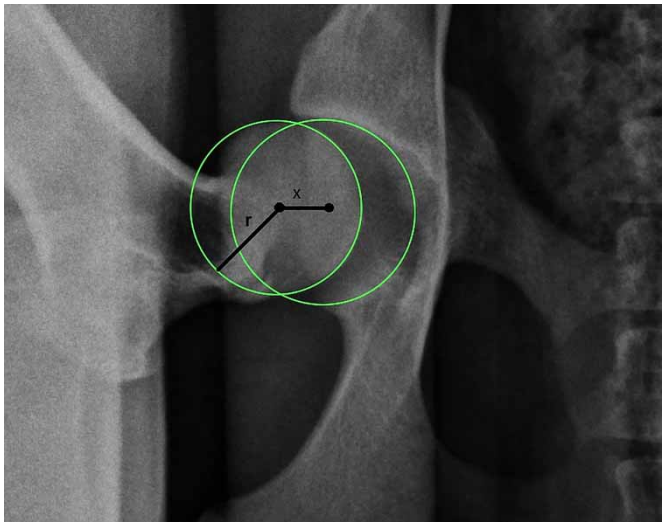

Figure 2. Radiograph showing measurements used for evaluation of the distraction index, calculated as the ratio of the distraction between the centres of the acetabulum and femoral head (x) to the radius of the femoral head (r), when a distraction force is applied to the sedated/anaesthetised patient as shown in Figure 1.

development on the extended-hip view results in the dog being classified as having CHD (Anonymous 2013). Of the three PennHIP radiographic views, the distraction view is most frequently utilised in genetic studies because it quantifies passive joint laxity, which has been widely recognised for its important role in the pathophysiology of CHD.

Heritability and breeding selection for a superior hip phenotype

Genetic gain through selective breeding is a product of the heritability of a trait and the selection pressure applied over generations. The selection pressure is related to the extent of phenotypic variation and the intensity of selection set by dog breeders. CHD scoring systems were introduced to assist dog breeders with the goal of reducing the prevalence and severity of hip dysplasia in future generations. The key assumption in any phenotypic scoring scheme is that successive generations will benefit from the selection pressure exerted against the trait in their parents and therefore, a better phenotype will be produced over time.

Heritability measures the extent to which offspring resemble their parents for a certain trait. Estimation of heritability uses statistical techniques to determine the extent to which relatives resemble each other for a particular trait (Nicholas 2010a). Heritability ranges from 0–1. If the heritability is 0, it means that relatives do not resemble each other at all for the trait of interest. Conversely, a trait with heritability of 1 is completely genetically determined. Traits with heritability less than 0.1 are considered lowly heritable; 0.2–0.3 moderately heritable and 0.4–1.0 to be highly heritable (Mackenzie 1985). The practical importance is that if the heritability is more than 0, then it should be possible to decrease the prevalence of a particular trait via selective breeding. In general, the higher the heritability, the greater the influence of genetic effects on the trait and thus the greater the potential response to breeding selection pressures (Mackenzie 1985; Nicholas 2010a). Heritability for the same trait may vary from one estimate to another. Estimates may differ due to sampling variation, the phenotype (method of hip scoring) being examined, the breed or population involved, the degree of inbreeding, environmental factors, and the method of calculation (Mackenzie 1985; Nicholas 2010a).

Historically, depending on the method of evaluation, the estimated heritability of CHD has been found to be >0.22–0.25, meaning that no less than approximately 22% of the disease is genetically controlled (Leighton *et al.* 1977; Fox *et al.* 1987). Tables 2–4 provide a non-exhaustive overview of the reported estimated breed heritabilities based on OFA, FCI and BVA scoring systems. The heritability estimates in these studies were performed using a variety of methods such as regression, Bayesian and/or Restricted Maximal Likelihood analyses. As a general rule, traits with heritability estimates >0.15 are considered to be under adequate genetic influence such that sufficient response will be seen with selective breeding (Wilson *et al.* 2011), thus decreasing the prevalence of the disease. Heritability estimates of previous studies performed on the OFA, FCI and BVA scoring systems have generally met or exceeded this level. To the author's knowledge, there have been no estimates of heritability performed specifically for dogs scored under the NZVA CHD Scheme, but, because the NZVA CHD Scheme is based on the BVA

Table 2. Reported heritabilities (h^2) for the Orthopaedic Foundation for Animals hip grading system for canine hip dysplasia, using the hip-extended radiographic view (subjective scoring system).

Breed	h^2 (SE)	No. dogs	Study
Bernese Mountain Dog	0.30 (0.04)	4,151	Reed *et al.* (2000)
Chinese Shar-pei	0.31 (0.05)	3,360	Reed *et al.* (2000)
English Setter	0.17 (0.05)	3,876	Reed *et al.* (2000)
German Shepherd Dog	0.22 (0.06)	1,186	Leighton *et al.* (1977)
German Shepherd Dog	0.43	575	Mackenzie *et al.* (1985)
Labrador Retriever	0.21 (0.006)	154,352	Hou *et al.* (2010)
Portuguese Water Dog	0.30 (0.06)	1,337	Reed *et al.* (2000)
Pooled h^2 for 17 breeds	0.76	2,716	Zhang *et al.* (2009)
Pooled h^2 for 74 breeds	0.22 (0.002)	760,455	Hou *et al.* (2013)

Table 3. Reported heritabilities (h^2) for the Fédération Cynologique Internationale hip grading system for canine hip dysplasia, using the hip-extended radiographic view (subjective scoring system).

Breed	h^2 (SE)	No. dogs	Study
Bernese Mountain Dog	0.42 (0.03)	8,221	Malm *et al.* (2008)
Bernese Mountain Dog	0.31 (0.06)	1,479	Lavrijsen *et al.* (2014)
Estrela Mountain Dog	0.3–0.43[a]	313	Silvestre *et al.* (2007)
German Shepherd Dog	0.31–0.35[a]	10,335	Leppänen *et al.* (2000b)
German Shepherd Dog	0.24–0.26[a]	21,371	Hamann *et al.* (2003)
German Shepherd Dog	0.25 (0.01)	47,730	Stock *et al.* (2011)
Golden Retriever	0.17 (0.03)	22,934	Lingaas and Klemetsdal (1990)
Golden Retriever	0.18 (0.04)	2,412	Lavrijsen *et al.* (2014)
Labrador Retriever	0.44	664	Ohlerth *et al.* (2001)
Labrador Retriever	0.24–0.29[a]	3,151	Vostrý *et al.* (2012)
Labrador Retriever	0.10 (0.03)	3,746	Lavrijsen *et al.* (2014)
Rottweiler	0.58 (0.04)	2,764	Mäki *et al.* (2000)
Rottweiler	0.38 (0.02)	14,693	Malm *et al.* (2008)
Newfoundland	0.26–0.28[a]	1,372	Dietschi *et al.* (2003)
Newfoundland	0.23 (0.08)	788	Lavrijsen *et al.* (2014)

[a] Heritability value varies with model and method of estimation.

Table 4. Reported heritabilities (h^2) for the British Veterinary Association hip scoring system for canine hip dysplasia, using the hip-extended radiographic view (semi-subjective scoring system).

Breed	h^2 (SE)	No. dogs	Study
Akita	0.39 (0.053)[a]	152	Lewis *et al.* (2013)
Bearded Collie	0.46 (0.048)[a]	350	Lewis *et al.* (2013)
Bernese Mountain Dog	0.36 (0.040)[a]	450	Lewis *et al.* (2013)
Border Collie	0.44 (0.033)[a]	1,008	Lewis *et al.* (2013)
English Setter	0.35 (0.049)[a]	198	Lewis *et al.* (2013)
Flat-coated Retriever	0.74 (0.25)	1,258	Wood *et al.* (2000a)
Flat-coated Retriever	0.28 (0.032)[a]	1,121	Lewis *et al.* (2013)
German Shepherd Dog	0.30 (0.02)[b]	13,124	Wilson *et al.* (2012)
German Shepherd Dog	0.35 (0.015)[a]	3,680	Lewis *et al.* (2013)
Golden Retriever	0.40 (0.017)[a]	5,374	Lewis *et al.* (2013)
Gordon Setter	0.20–0.38[c]	1,152	Wood *et al.* (2000b)
Gordon Setter	0.43 (0.062)[a]	175	Lewis *et al.* (2013)
Labrador Retriever	0.34 (0.02)	13,382	Wood *et al.* (2002)
Labrador Retriever	0.35 (0.016)[a] 0.50 (0.018)[d]	25,243	Lewis *et al.* (2010)
Labrador Retriever	0.35 (0.02)	25,243	Woolliams *et al.* (2011)
Labrador Retriever	0.33 (0.012)[a]	17,164	Lewis *et al.* (2013)
Newfoundland	0.49 (0.08)	1,566	Wood *et al.* (2000a)
Newfoundland	0.46 (0.041)[a]	478	Lewis *et al.* (2013)
Rhodesian Ridgeback	0.33 (0.048)[a]	541	Lewis *et al.* (2013)
Rottweiler	0.39 (0.028)[a]	616	Lewis *et al.* (2013)
Siberian Husky	0.48 (0.038)[a]	300	Lewis *et al.* (2013)
Tibetan Terrier	0.34 (0.048)[a]	757	Lewis *et al.* (2013)

[a] Heritability estimate performed on hip scores transformed onto a logarithmic scale.
[b] Heritability estimate study based on the Australian Veterinary Association hip scoring system, which is similar to the BVA system.
[c] Heritability value varies with model and method of estimate.
[d] Heritability estimate performed on original, untransformed hip score.

hip scoring system, it is possible to infer the heritability of the NZVA hip phenotype from the BVA hip phenotype.

While a thorough quantitative genetic analysis of the entire PennHIP database has not been published, a small number of studies using the distraction index have been performed. Todhunter *et al.* (2003) found the heritability of the distraction index in 147 Labrador Retrievers across four generations to be 0.5. A larger study by Zhang *et al.* (2009) comprising 2,716 dogs across 17 breeds reported a heritability of 0.61 for the distraction index. A recent genetic analysis of the distraction index in the Estrela Mountain dog, using a linear animal model, reported a very high heritability of 0.83 (Ginja *et al.* 2008). This estimate was based only on 215 observations and has an SE of 0.11. As heritability is unique to the phenotype and population in which it is estimated (Mackenzie 1985), this high heritability estimate from an atypical breed cannot be directly applied to other breeds.

Effectiveness of the radiological scoring systems in lowering the prevalence of CHD

Several authors have commented that despite >40 years of radiographic screening, the prevalence of CHD remains high and have questioned the efficacy of the schemes or programmes adopted by the OFA, FCI and BVA (e.g. Leppanen *et al.* 2000a; Verhoeven *et al.* 2012). There are somewhat conflicting reports as to the efficacy of the OFA scheme. One evaluation of the OFA database showed a steady, albeit slow, increase in the proportions of dogs graded as excellent and good, whereas proportions of fair and mild/moderate/severe dysplastic grades significantly decreased over the period 1989–2003 (Kaneene *et al.* 2009). More recently, Hou *et al.* (2013) performed an estimated breeding value (EBV) analysis on 760,455 hip scores across 74 breeds listed in the OFA database to evaluate genetic trends between the period 1970–2009 inclusive. The study found a genetic improvement of 0.1 units of hip score during the study period, which was equivalent to 16.4% of the phenotypic standard deviation. These values corresponded to a 0.52% decrease in incidence of CHD in the study population. Additionally, the study emphasised that while some genetic improvement was evident on the basis of the EBV analysis of the OFA database, there was a variation in the amount of genetic improvement amongst breeds (Hou *et al.* 2013). These studies suggest that whilst the OFA system has been effective at reducing the number of severely affected dogs, there has been only limited progress towards reducing the overall impact of CHD.

A genetic evaluation of the effectiveness of the BVA scoring system in reducing the prevalence of CHD in UK Labrador Retrievers reported a genetic progress of 0.376 untransformed (or 0.155 log-transformed) hip score units per annum (Lewis *et al.* 2010). This translates to a 1.4% decline year on year or a 13% improvement in hip scores over the 10-year study period. The authors concluded that this was very minimal progress against CHD, and was equivalent to only avoiding 15% of the

worst animals for breeding. More recently, an EBV analysis on 142,287 hip scores across fifteen breeds listed on the BVA CHD database evaluated the genetic improvement made when breeding selection was carried out on the basis of phenotypic scores (Lewis *et al.* 2013). Regression of the EBV on the date of birth revealed that 14/15 breeds exhibited some genetic improvement during the study period. The authors discussed that despite the significant genetic progress, the extent of improvement was only small with a 0.13% to 1.98% decline of hip scores per year, indicating a low selection intensity was employed throughout the study period (Lewis *et al.* 2013). To the authors' knowledge, no genetic studies have been conducted on the efficacy of the NZVA CHD scheme at reducing the prevalence of CHD. However, an evaluation of the phenotypic trend of the NZVA hip scores in four populous breeds of dogs revealed a small but significant phenotypic trend towards an improved radiographic hip conformation in German Shepherd dogs, but not in the Labrador Retrievers, Golden Retrievers or Rottweilers (Worth *et al.* 2011). However, the chosen method of regression analysis based on individual animal hip scores may have overlooked the genetic gain made in some lines within breeds, by not evaluating the genetic trend.

Significant selection bias has been reported in the OFA system with radiographs of normal-appearing hips being 8.2 times more likely to be submitted by veterinarians than radiographs that showed the dogs were clearly dysplastic (Paster *et al.* 2005); a process termed pre-screening. Pre-screening is a criticism of most CHD scoring schemes and skews the population of scored dogs by removing the worst-affected individuals (Paster *et al.* 2005). Submission of radiographs is voluntary in all but a few countries. In New Zealand, there is no compulsion to submit all radiographs performed for the purpose of scoring and, anecdotally, pre-screening does occur. There is also no legal requirement to hip score dogs that are to be used for breeding. Additionally, when a lame dog is diagnosed with clinical CHD, a radiologic score is not captured by any database. Thus, the published average hip scores are not a true reflection of the disease prevalence or severity within a given breed. The quality of radiographs also has a significant effect on the ability of any assessor to accurately determine a dog's CHD radiological phenotype. Thus the credibility of screening methods for CHD using the extended-hip view is questionable (Verhoeven *et al.* 2009).

The use of radiological scoring methods in countries or breeding colonies with mandatory scoring programmes has been reported to be more successful at lowering the prevalence of CHD (Hedhammar *et al.* 1979; Swenson *et al.* 1997; Genevois *et al.* 2008). In Sweden (which uses the FCI method of hip scoring), it has been mandatory since 1984 for the hip joint status of both parents to be published before the Swedish Kennel Club will register the puppies of that mating. This open registration and mandatory scoring may have contributed to the observed improvement in the median score for CHD of several breeds in Sweden (Swenson *et al.* 1997).

As previously discussed, the higher the heritability of a trait, the larger the contribution of genetic factors to the resultant phenotype and thus the greater the response to selection (Mackenzie 1985; Nicholas 2010b). While a thorough genetic evaluation of the PennHIP database has yet to be conducted, preliminary studies suggest that the PennHIP distraction index phenotype potentially has a higher heritability than the hip-extended radiographic phenotype and could therefore yield a better response to selection than the OFA, FCI or BVA phenotypes. This is because higher heritability indicates that a larger proportion of the phenotype is genetically determined and therefore more susceptible to manipulation by selective breeding to decrease the prevalence of disease, given adequate selection intensity. At present, no national veterinary association has adopted the PennHIP method as the basis for recommendations regarding the use of breeding stock.

Discussion

The small amount of genetic progress attained using selection of breeding stock based on individual extended-hip view phenotype has led several commentators to recommend the use of EBV in CHD breeding schemes (Hou *et al.* 2013; Lewis *et al.* 2013). Selection of breeding stock solely on the basis of their individual phenotypic hip status is not the most accurate method of identifying dogs with superior genes, because for a quantitative trait like CHD, it is possible for two dogs of identical genotypes to express very different phenotypes under differing environmental influences (Lust and Farrell 1977). A dog with phenotypically better hips may not have better genes for transmission to its offspring as the favourable hip score may have been a result of a better environment. Instead of the phenotypic hip score or grade, the identification of dogs with superior genes is best determined using EBV. The EBV is a measure of the genetic superiority of an animal as compared to its counterparts and is calculated from the phenotypes of the individual, their relatives and pedigree data (Nicholas 2010a). The EBV is a more accurate predictor of an individual's genetic merit because it takes into account the genetic contribution of superior genes from all relatives (such as offspring or siblings) as well as any other available information about the individual in question (Wilson *et al.* 2011; Woolliams *et al.* 2011). The accuracy of an individual's EBV increases as information becomes available from its relatives. EBV confers greater selection power allowing accelerated genetic gain over time, compared to using individual phenotypic scores (Lewis *et al.* 2010; Keller *et al.* 2011).

In a population of German Shepherd dogs, selection procedures based on breeding values were more efficient than selection schemes based on phenotypic records of parents (FCI hip scoring) (Janutta *et al.* 2008). In another study, it was estimated that it would take approximately 44 years to decrease the median hip score from 10 to 5 if identification of dogs for breeding were to continue on the basis of the phenotypic selection (BVA hip scores). In contrast, by utilising an EBV-based selection scheme to identify dogs with superior genes, it would take approximately 37 years (19% faster) to achieve the same amount of improvement in the BVA hip scores (Lewis *et al.* 2010). Similarly, in a range of simulated scenarios (e.g. large *vs.* small population; low *vs.* high prevalence of CHD), the average genetic gain attained from selection based on Best Linear Unbiased Prediction (estimated) breeding value was 1.03–1.25 times higher than selection based on phenotype (FCI hip scores) alone (Malm *et al.* 2013). Additionally, because the accuracy of breeding selection is directly correlated with the extent of genetic progress, higher selection accuracy will result in greater genetic improvement towards better hip conformation. This was demonstrated in a study Lewis *et al.* (2013), whereby the mean accuracy of selection based on individual or parental phenotype (BVA hip score) was found to be between 1.16 and 1.30, as compared to the higher mean accuracy of 1.44 when

selection was made on the basis of EBV (Lewis *et al.* 2013). In a simulated study population of German Shepherd dogs, breeding selection based on EBV was up to three times more efficient in achieving genetic progress than selection on phenotype alone; however, the study also revealed that an even higher response to selection was obtained via genomic selection (Stock and Distl 2010). Genomic selection has been shown to be the most superior method breeding selection, as compared to EBV or phenotypic selection, in a number of simulated populations (Stock and Distl 2010; Sánchez-Molano *et al.* 2014). However, there is only limited use of DNA marker technology at present (Woolliams *et al.* 2011) whilst it is still undergoing further development and refinement for routine clinical use (see above discussion). Therefore, in the short term at least, it is the authors' view that breeding selection on the basis of EBV remains the next best alternative.

Estimated breeding values can be generated for dogs that have not been hip scored, as long as they have relatives within their pedigree that have been previously scored. This allows an EBV-based selection of breeding stock to be carried out even if not all animals within the breeding population have been scored. This also means that utilising the available information from relatives will allow the EBV of a puppy to be calculated the moment it is born (Lewis *et al.* 2010); this is beneficial as it allows breeders to plan ahead as well as potentially assisting with the process and progress of selection. Another major advantage for the utilisation of EBV for breeding selection is that EBV are corrected for identifiable non-genetic (environmental) effects which may cause bias on the hip score (Lewis *et al.* 2010; Wilson *et al.* 2011; Woolliams *et al.* 2011).

The use of a phenotypic screening test with a higher heritability than the current extended-hip view phenotype would aid an EBV scheme for CHD. Although published studies suggest the heritability of the distraction index is higher than the heritability of the extended-hip view, only a limited number of genetic analyses have been performed on the distraction index to date. The authors are hopeful that a heritability estimate of the distraction index based on a larger dataset will be available in the near future, because using a hip phenotype with a high heritability in an EBV-based selection scheme will likely accelerate the rate of genetic progress, compared to hip phenotypes with lower heritability.

Conclusion

Canine hip dysplasia is a multifactorial trait with a moderate to high heritability. By applying selection pressure appropriately, a reduction in the prevalence of CHD should be achievable. Despite many decades of use, selection using traditional radiological phenotypic scoring schemes has had only modest success. Selection of dogs for breeding on the basis of EBV may prove more effective at reducing the prevalence of CHD than selection based on individual hip scores/grades. The incorporation of EBV into selective breeding programmes will also enable genetic trends to be monitored prospectively and as dynamically as possible in all populations under selection.

Declaration of interest

Andrew Worth is the current Convenor of the NZVA Dysplasia Schemes and receives an honorarium for this position. He is also a PennHIP-certified veterinarian, whose training was supported by the New Zealand Police.

References

*Anonymous. *Orthopedic Foundation for Animals. An Examination of Hip Grading.* http://www.offa.org/hd_grades.html (accessed 24 February 2014). Orthopedic Foundation for Animals, Columbia, MO, USA, 2010

*Anonymous. *Interpretation of the NZVA Hip Dysplasia Scheme Scoring System.* http://www.nzva.org.nz/sites/default/files/domain-0/Interpretation%20of%20Hip%20Dysplasia%20Grade%20-%202011.pdf (accessed 24 February 2014). New Zealand Veterinary Association, Wellington, NZ, 2011

*Anonymous. *PennHIP Hip Improvement Program.* http://info.antechimagingservices.com/pennhip/navigation/general/what-is-PennHIP.html (accessed 25 February 2014). ANTECH Imaging Services, Irvine, CA, USA, 2013

Bliss S, Todhunter RJ, Quaas R, Casella G, Wu R, Lust G, Williams AJ, Hamilton S, Dykes NL, Yeager A, *et al.* Quantitative genetics of traits associated with hip dysplasia in a canine pedigree constructed by mating dysplastic Labrador Retrievers with unaffected greyhounds. *American Journal of Veterinary Research* 63, 1029–35, 2002

Cardinet GH 3rd, Kass PH, Wallace LJ, Guffy MM. Association between pelvic muscle mass and canine hip dysplasia. *Journal of the American Veterinary Medical Association* 210, 1466–73, 1997

Comhaire FH, Snaps F. Comparison of two canine registry databases on the prevalence of hip dysplasia by breed and the relationship of dysplasia with body weight and height. *American Journal of Veterinary Research* 69, 330–3, 2008

*Cook JL, Tomlinson JL, Constantinescu GM. Pathophysiology, diagnosis, and treatment of canine hip dysplasia. *Compendium on Continuing Education for the Practicing Veterinarian* 18, 853–66, 1996

Culp WTN, Kapatkin AS, Gregor TP, Powers MY, McKelvie PJ, Smith GK. Evaluation of the Norberg angle threshold: a comparison of Norberg angle and distraction index as measures of coxofemoral degenerative joint disease susceptibility in seven breeds of dogs. *Veterinary Surgery* 35, 453–9, 2006

Dennis R. Interpretation and use of BVA/KC hip scores in dogs. *In Practice* 34, 178–94, 2012

Dietschi E, Schawalder P, Gaillard C. Estimation of genetic parameters for canine hip dysplasia in the Swiss Newfoundland population. *Journal of Animal Breeding and Genetics* 120, 150–61, 2003

Flückiger MA. Scoring radiographs for canine hip dysplasia – the big three organizations of the world. *European Journal of Companion Animal Practice* 17, 135–40, 2007

Fox SM, Burns J, Burt J. The dysplastic hip: a crippling problem in dogs. *Veterinary Medicine* 82, 684–93, 1987

Friedenberg SG, Zhu L, Zhang Z, Foels WvdB, Schweitzer PA, Wang W, Fisher PJ, Dykes NL, Corey E, Vernier-Singer M, *et al.* Evaluation of a fibrillin 2 gene haplotype associated with hip dysplasia and incipient osteoarthritis in dogs. *American Journal of Veterinary Research* 72, 530–40, 2011

Frost HM. Pathogenesis of congenital hip dysplasia (CHD). A proposal. *Veterinary and Comparative Orthopaedics and Traumatology* 1, 1–10, 1989

Genevois JP, Remy D, Viguier E, Carozzo C, Collard F, Cachon T, Maitre P, Fau D. Prevalence of hip dysplasia according to official radiographic screening, among 31 breeds of dogs in France. *Veterinary and Comparative Orthopaedics and Traumatology* 21, 21–4, 2008

Ginja MMD, Silvestre AM, Ferreira AJA, Gonzalo-Orden JM, Orden MA, Melo-Pinto P, Llorens-Pena MP, Colaco J. Passive hip laxity in Estrela Mountain dog – distraction index, heritability and breeding values. *Acta Veterinaria Hungarica* 56, 303–12, 2008

Guo G, Zhou Z, Wang Y, Zhao K, Zhu L, Lust G, Hunter L, Friedenberg S, Li J, Zhang Y, *et al.* Canine hip dysplasia is predictable by genotyping. *Osteoarthritis and Cartilage* 19, 420–9, 2011

Hamann H, Kirchhoff T, Distl O. Bayesian analysis of heritability of canine hip dysplasia in German Shepherd dogs. *Journal of Animal Breeding and Genetics* 120, 258–68, 2003

Hedhammar A, Olsson SE, Andersson SA, Persson L, Pettersson L, Olausson A, Sundgren PE. Canine hip dysplasia: study of heritability in 401 litters of German Shepherd dogs. *Journal of the American Veterinary Medical Association* 174, 1012–6, 1979

Henricson B, Norberg I, Olssons SE. On the etiology and pathogenesis of hip dysplasia: a comparative review. *Journal of Small Animal Practice* 7, 673–88, 1966

Henry GA. Radiographic development of canine hip dysplasia. *Veterinary Clinics of North America: Small Animal Practice* 22, 559–78, 1992

Hou Y, Wang Y, Lust G, Zhu L, Zhang Z, Todhunter RJ. Retrospective analysis for genetic improvement of hip joints of cohort labrador retrievers in the United States: 1970–2007. *PLoS One* 5, e9410, 2010

Hou Y, Wang Y, Lu X, Zhang X, Zhao Q, Todhunter RJ, Zhang Z. Monitoring hip and elbow dysplasia achieved modest genetic improvement of 74 dog breeds over 40 years in USA. *PLoS One* 8, e76390, 2013

Hunter AC. Radiography for hip dysplasia evaluation. *New Zealand Veterinary Journal* 34, 43–5, 1986

Hutt FB. Genetic selection to reduce the incidence of hip dysplasia in dogs. *Journal of the American Veterinary Medical Association* 151, 1041–8, 1967

Ihemelandu EC, Cardinet GHr, Guffy MM, Wallace LJ. Canine hip dysplasia: differences in pectineal muscles of healthy and dysplastic German Shepherd dogs when two months old. *American Journal of Veterinary Research* 44, 411–6, 1983

Janutta V, Distl O. Inheritance of canine hip dysplasia: Review of estimation methods and of heritability estimates and prospects on further developments. *Deutsche tierarztliche Wochenschrift* 113, 6–12, 2006

Janutta V, Hamann H, Distl O. Genetic and phenotypic trends in canine hip dysplasia in the German population of German shepherd dogs. *Berliner Und Munchener Tierarztliche Wochenschrift* 121, 102–9, 2008

Kaneene JB, Mostosky UV, Miller R. Update of a retrospective cohort study of changes in hip joint phenotype of dogs evaluated by the OFA in the United States, 1989–2003. *Veterinary Surgery* 38, 398–405, 2009

Kealy RD, Olsson SE, Monti KL, Lawler DF, Biery DN, Helms RW, Lust G, Smith GK. Effects of limited food consumption on the incidence of hip dysplasia in growing dogs. *Journal of the American Veterinary Medical Association* 201, 857–63, 1992

Kealy RD, Lawler DF, Monti KL, Biery D, Helms RW, Lust G, Olsson SE, Smith GK. Effects of dietary electrolyte balance on subluxation of the femoral head in growing dogs. *American Journal of Veterinary Research* 54, 555–62, 1993

Keller GG, Dziuk E, Bell JS. How the orthopedic foundation for animals (OFA) is tackling inherited disorders in the USA: using hip and elbow dysplasia as examples. *Veterinary Journal* 189, 197–202, 2011

Krontveit RI, Trangerud C, Sævik BK, Skogmo HK, Nødtvedt A. Risk factors for hip-related clinical signs in a prospective cohort study of four large dog breeds in Norway. *Preventive Veterinary Medicine* 103, 219–27, 2012

Lavrijsen ICM, Heuven HCM, Meij BP, Theyse LFH, Nap RC, Leegwater PAJ, Hazewinkel HAW. Prevalence and co-occurrence of hip dysplasia and elbow dysplasia in Dutch pure-bred dogs. *Preventive Veterinary Medicine* 114, 114–22, 2014

Leighton EA, Linn JM, Willham RL, Castleberry MW. A genetic study of canine hip dysplasia. *American Journal of Veterinary Research* 38, 241–4, 1977

Leppänen M, Maki K, Juga J, Saloniemi H. Factors affecting hip dysplasia in German Shepherd dogs in Finland: efficacy of the current improvement programme. *Journal of Small Animal Practice* 41, 19–23, 2000a

Leppänen M, Mäki K, Juga J, Saloniemi H. Estimation of heritability for hip dysplasia in German Shepherd dogs in Finland. *Journal of Animal Breeding and Genetics* 117, 97–103, 2000b

Lewis TW, Blott SC, Woolliams JA. Genetic evaluation of hip score in UK Labrador Retrievers. *PLoS One* 5, e12797, 2010

Lewis TW, Blott SC, Woolliams JA. Comparative analyses of genetic trends and prospects for selection against hip and elbow dysplasia in 15 UK dog breeds. *BMC Genetics* 14, 16, 2013

Lingaas F, Klemetsdal G. Breeding values and genetic trend for hip dysplasia in the Norwegian golden retriever population. *Journal of Animal Breeding and Genetics* 107, 437–43, 1990

Lust G, Farrell PW. Hip dysplasia in dogs: the interplay of genotype and environment. *Cornell Veterinarian* 67, 447–67, 1977

Lust G, Beilman WT, Rendano VT. A relationship between degree of laxity and synovial fluid volume in coxofemoral joints of dogs predisposed for hip dysplasia. *American Journal of Veterinary Research* 41, 55–60, 1980

Mackenzie SA. Why heritability estimates differ: canine hip dysplasia. *Canine Practice* 12, 19–22, 1985

Mackenzie SA, Oltenacu EAB, Leighton EA. Heritability estimate for temperament scores in German shepherd dogs and its genetic correlation with hip dysplasia. *Behavior Genetics* 15, 475–82, 1985

Mäki K, Liinamo AE, Ojala M. Estimates of genetic parameters for hip and elbow dysplasia in finnish rottweilers. *Journal of Animal Science* 78, 1141–8, 2000

Malm S, Fikse WF, Danell B, Strandberg E. Genetic variation and genetic trends in hip and elbow dysplasia in Swedish Rottweiler and Bernese Mountain dog. *Journal of Animal Breeding and Genetics* 125, 403–12, 2008

Malm S, Sørensen AC, Fikse WF, Strandberg E. Efficient selection against categorically scored hip dysplasia in dogs is possible using best linear unbiased prediction and optimum contribution selection: a simulation study. *Journal of Animal Breeding and Genetics* 130, 154–64, 2013

Marschall Y, Distl O. Mapping quantitative trait loci for canine hip dysplasia in German Shepherd dogs. *Mammalian Genome* 18, 861–70, 2007

*__Morgan JP, Stephens M__. *Radiographic Diagnosis and Control of Canine Hip Dysplasia*. Iowa State University Press, Ames, USA, 1985

*__Nicholas FW__. Quantitative variation. In: *Introduction to Veterinary Genetics*. 3rd Edtn. Pp 216–29. Wiley-Blackwell, Chichester, UK, 2010a

*__Nicholas FW__. Familial disorders not due to a single gene. In: *Introduction to Veterinary Genetics*. 3rd Edtn. Pp 139–150. Wiley-Blackwell, Chichester, UK, 2010b

Ohlerth S, Lang J, Busato A, Gaillard C. Estimation of genetic population variables for six radiographic criteria of hip dysplasia in a colony of Labrador Retrievers. *American Journal of Veterinary Research* 62, 846–52, 2001

Paster ER, LaFond E, Biery DN, Iriye A, Gregor TP, Shofer FS, Smith GK. Estimates of prevalence of hip dysplasia in golden retrievers and Rottweilers and the influence of bias on published prevalence figures. *Journal of the American Veterinary Medical Association* 226, 387–92, 2005

Pfahler S, Distl O. Identification of quantitative trait loci (QTL) for canine hip dysplasia and canine elbow dysplasia in Bernese Mountain dogs. *PLoS One* 7, e49782, 2012

Reed AL, Keller GG, Vogt DW, Ellersieck M, Corley EA. Effect of dam and sire qualitative hip conformation scores on progeny hip conformation. *Journal of the American Veterinary Medical Association* 217, 675–80, 2000

Rendano VT, Ryan G. Canine hip dysplasia evaluation. *Veterinary Radiology* 26, 170–86, 1985

Riser WH. A new look at developmental subluxation and dislocation: hip dysplasia in the dog. *Journal of Small Animal Practice* 4, 421–34, 1963

Riser WH. Hip dysplasia as a disease. *Veterinary Pathology* 12, 316–23, 1975a

Riser WH. Observations and research on hip dysplasia. *Veterinary Pathology* 12, 239–63, 1975b

Riser WH. The dysplastic hip joint: radiologic and histologic development. *Veterinary Pathology* 12, 279–305, 1975c

Sánchez-Molano E, Woolliams JA, Blott SC, Wiener P. Assessing the impact of genomic selection against hip dysplasia in the labrador retriever dog. *Journal of Animal Breeding and Genetics* 131, 134–45, 2014

*__Schnelle GB__. Congenital subluxation of the coxofemoral joint in a dog. *University of Pennsylvania Bulletin* 65, 15–6, 1937

Silvestre AM, Ginja MMD, Ferreira AJA, Colaço J. Comparison of estimates of hip dysplasia genetic parameters in Estrela Mountain dog using linear and threshold models. *Journal of Animal Science* 85, 1880–4, 2007

Smith GK, Biery DN, Gregor TP. New concepts of coxofemoral joint stability and the development of a clinical stress-radiographic method for quantitating hip joint laxity in the dog. *Journal of the American Veterinary Medical Association* 196, 59–70, 1990

Smith GK, Popovich CA, Gregor TP. Evaluation of factors contributing to the risk of developing degernative joint disease associated with hip dysplasia in dogs. *Journal of the American Veterinary Medical Association* 206, 642–7, 1995

Smith GK, Paster ER, Powers MY, Lawler DF, Biery DN, Shofer FS, McKelvie PJ, Kealy RD. Lifelong diet restriction and radiographic evidence of osteoarthritis of the hip joints in dogs. *Journal of the American Veterinary Medical Association* 229, 690–3, 2006

Smith GK, Lawler DF, Biery DN, Powers MY, Shofer FS, Gregor TP, Karbe GT, McDonald-Lynch MB, Evans RH, Kealy RD. Chronology of hip dysplasia development in a cohort of 48 labrador retrievers followed for life. *Veterinary Surgery* 41, 20–33, 2012

Steinetz BG, Williams AJ, Lust G, Schwabe C, Büllesbach EE, Goldsmith LT. Transmission of relaxin and estrogens to suckling canine pups via milk and possible association with hip joint laxity. *American Journal of Veterinary Research* 69, 59–67, 2008

Stock KF, Distl O. Simulation study on the effects of excluding offspring information for genetic evaluation versus using genomic markers for selection in dog breeding. *Journal of Animal Breeding and Genetics* 127, 42–52, 2010

Stock KF, Klein S, Tellhelm B, Distl O. Genetic analyses of elbow and hip dysplasia in the German shepherd dog. *Journal of Animal Breeding and Genetics* 128, 219–29, 2011

Swenson L, Audell L, Hedhammar A. Prevalence and inheritance of and selection for hip dysplasia in seven breeds of dogs in Sweden and benefit: cost analysis of a screening and control program. *Journal of the American Veterinary Medical Association* 210, 207–14, 1997

*Todhunter RJ, Lust G. Hip dysplasia: pathogenesis. In: Slatter DH. (ed). *Textbook of Small Animal Surgery*. 3rd Edtn. Pp 2009–19. Saunders, Philadelphia PA, USA, 2003

Todhunter RJ, Bliss SP, Casella G, Wu R, Lust G, Burton-Wurster NI, Williams AJ, Gilbert RO, Acland GM. Genetic structure of susceptibility traits for hip dysplasia and microsatellite informativeness of an outcrossed canine pedigree. *Journal of Heredity* 94, 39–48, 2003

Todhunter RJ, Mateescu R, Lust G, Burton-Wurster NI, Dykes NL, Bliss SP, Williams AJ, Vernier-Singer M, Corey E, Harjes C, *et al*. Quantitative trait loci for hip dysplasia in a cross-breed canine pedigree. *Mammalian genome* 16, 720–30, 2005

Tomlinson JL, Johnson JC. Quantification of measurement of femoral head coverage and Norberg angle within and among four breeds of dogs. *American Journal of Veterinary Research* 61, 1492–500, 2000

Verhoeven G, Coopman F, Duchateau L, Saunders JH, Van Rijssen B, Van Bree H. Interobserver agreement in the diagnosis of canine hip dysplasia using the standard ventrodorsal hip-extended radiographic method. *Journal of Small Animal Practice* 48, 387–93, 2007

Verhoeven GEC, Coopman F, Duchateau LUC, Bosmans TIM, Van Ryssen B, Van Bree H. Interobserver agreement on the assessability of standard ventrodorsal hip-extended radiographs and its effect on agreement in the diagnosis of canine hip dysplasia and on routine FCI scoring. *Veterinary Radiology and Ultrasound* 50, 259–63, 2009

Verhoeven G, Fortrie R, Van Ryssen B, Coopman F. Worldwide screening for canine hip dysplasia: where are we now? *Veterinary Surgery* 41, 10–9, 2012

Vostrý L, Čapková Z, Šebková N, Přibyl J. Estimation of genetic parameters for hip dysplasia in Czech Labrador Retrievers. *Journal of Animal Breeding and Genetics* 129, 60–9, 2012

Wilson B, Nicholas FW, Thomson PC. Selection against canine hip dysplasia: success or failure? *Veterinary Journal* 189, 160–8, 2011

Wilson BJ, Nicholas FW, James JW, Wade CM, Tammen I, Raadsma HW, Castle K, Thomson PC. Heritability and phenotypic variation of canine hip dysplasia radiographic traits in a cohort of Australian German shepherd dogs. *PLoS One* 7, e39620, 2012

Wood JLN, Lakhani KH, Dennis R. Heritability and epidemiology of canine hip-dysplasia score in flat-coated retrievers and Newfoundlands in the United Kingdom. *Preventive Veterinary Medicine* 46, 75–86, 2000a

Wood JLN, Lakhani KH, Dennis R. Heritability of canine hip dysplasia score and its components in Gordon Setters. *Preventive Veterinary Medicine* 46, 87–97, 2000b

Wood JLN, Lakhani KH, Rogers K. Heritability and epidemiology of canine hip dysplasia score and its components in Labrador Retrievers in the United Kingdom. *Preventive Veterinary Medicine* 55, 95–108, 2002

Woolliams JA, Lewis TW, Blott SC. Canine hip and elbow dysplasia in UK Labrador retrievers. *Veterinary Journal* 189, 169–76, 2011

Worth AJ, Laven RA, Erceg VH. An assessment of the agreement between the New Zealand veterinary association hip dysplasia scoring system and the PennHIP distraction index in German Shepherd dogs. *New Zealand Veterinary Journal* 57, 338–45, 2009

Worth AJ, Bridges JP, Jones G. Trends in the phenotypic hip status of selected breeds of dog as measured by the New Zealand veterinary association hip dysplasia scheme (1990–2008). *New Zealand Veterinary Journal* 59, 67–74, 2011

Zhang Z, Zhu L, Sandler J, Friedenberg SS, Egelhoff J, Williams AJ, Dykes NL, Hornbuckle W, Krotscheck U, Moise NS, *et al*. Estimation of heritabilities, genetic correlations, and breeding values of four traits that collectively define hip dysplasia in dogs. *American Journal of Veterinary Research* 70, 483–92, 2009

Zhou Z, Sheng X, Zhang Z, Zhao K, Zhu L, Guo G, Friedenberg SG, Hunter LS, Vandenberg-Foels WS, Hornbuckle WE, *et al*. Differential genetic regulation of canine hip dysplasia and osteoarthritis. *PLoS One* 5, e13219, 2010

Zhu L, Zhang Z, Feng F, Schweitzer P, Phavaphutanon J, Vernier-Singer M, Corey E, Friedenberg S, Mateescu R, Williams A, *et al*. Single nucleotide polymorphisms refine QTL intervals for hip joint laxity in dogs. *Animal Genetics* 39, 141–6, 2008

Zhu L, Zhang Z, Friedenberg S, Jung S-W, Phavaphutanon J, Vernier-Singer M, Corey E, Mateescu R, Dykes N, Sandler J, *et al*. The long (and winding) road to gene discovery for canine hip dysplasia. *Veterinary Journal* 181, 97–110, 2009

Submitted 22 November 2013

Accepted for publication 10 June 2014

First published online 29 July 2014