Breeding for Improved Hip and Elbow Health in Swedish Dogs

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Abstract

Decades of selective breeding to reduce the prevalence of hip and elbow dysplasia (HD and ED) in Swedish dogs, based on phenotypic assessment of radiographic hip status, has had limited success. The prevalence of dysplastic dogs is still high in many large-sized and giant breeds and among the most common causes for euthanasia and costly veterinary care in numerous breeds are joint-related problems. The aim of this thesis was to investigate the possibilities of more efficient breeding strategies for improved hip and elbow health in Swedish dogs by improving the genetic evaluation of HD and ED, and by evaluating the clinical significance of radiographic hip status.

Data from several different sources were combined in the analyses: pedigree information and screening records for HD and ED from the Swedish Kennel Club, questionnaire data about routines for hip and elbow screening from Swedish veterinary clinics and insurance data on hip-related veterinary care and mortality from Agria Insurance Company. Moreover, simulated data were used to evaluate selection strategies.

Radiographic hip status in young adult dogs was shown to be strongly associated with subsequent incidence of veterinary care and mortality related to the hip joint. Furthermore, the genetic analyses of screening records for HD and ED showed considerable genetic variation and moderate heritability of both traits. Taken together, these findings support the use of screening records for HD and ED in selection to reduce prevalence of clinical problems related to hip and elbow joints. However, the impact of systematic environmental factors, such as sedation method, on the phenotypic expression of HD and ED implies that the individual's screening result alone is an imprecise estimate of its breeding value. Simulation of selection strategies against HD showed that selection based on BLUP breeding values was superior to phenotypic selection, leading to faster genetic progress and more rapid reduction of dysplastic dogs. Based on the studies included in this thesis, it is concluded that implementation of breeding schemes based on BLUP breeding values, instead of phenotypic records, should be prioritised to enable a more efficient breeding for improved hip and elbow health in Swedish dogs.

Keywords: dog breeding, canine, hip dysplasia, elbow dysplasia, categorical traits, screening, genetic evaluation, selection, sedation, simulation

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Till Britta.
Jag önskar att du hade fått vara med hela vägen.

It should be a relatively easy matter to reduce the incidence of dysplasia of the hip in dogs to the point at which it becomes a rare disease.
Otto Schales, 1957

Contents

List of Publications

This thesis is based on the work contained in the following papers, referred to by Roman numerals in the text:

I Malm, S., Strandberg, E., Danell, B., Audell, L., Swenson L. and Hedhammar Å. (2007). Impact of sedation method on the diagnosis of hip and elbow dysplasia in Swedish dogs. *Prev. Vet. Med.* 78, 196-209.

II Malm, S., Fikse, W.F., Egenvall, A., Bonnett, B.N., Gunnarsson, L., Hedhammar, Å. and Strandberg, E. (2010). Association between radiographic assessment of hip status and subsequent incidence of veterinary care and mortality related to hip dysplasia in insured Swedish dogs. *Prev. Vet. Med.* 93, 222-232.

III Malm, S., Fikse, W.F., Danell, B. and Strandberg, E. (2008). Genetic variation and genetic trends in hip and elbow dysplasia in Swedish Rottweiler and Bernese Mountain Dog. *J. Anim. Breed. Genet.* 125, 403-412.

IV Malm, S., Sørensen, A.C., Fikse, W.F. and Strandberg, E. Efficient selection against categorically scored hip dysplasia in dogs is possible using BLUP and optimum contribution selection: a simulation study (submitted).

Paper I-III are reproduced with the permission of the publishers.

Abbreviations

BLUP	best linear unbiased prediction
BMD	Bernese Mountain Dog
DNA	deoxyribonucleic acid
EBV	estimated breeding value
ED	elbow dysplasia
FCI	Fédération Cynologique Internationale
FCP	fragmented coronoid process
GR	Golden Retriever
GSD	German Shepherd Dog
HD	hip dysplasia
IEWG	International Elbow Working Group
LR	Labrador Retriever
OCD	osteochondritis dissecans
OCS	optimum contribution selection
QTL	quantitative trait locus
RW	Rottweiler
SKC	the Swedish Kennel Club
SNP	single-nucleotide polymorphism
UAP	ununited anconeal process

Introduction

In Sweden there are about 730 000 dogs (Statistiska Centralbyrån, 2006) out of which approximately 70% are purebred and registered in the Swedish Kennel Club (SKC) (Swenson *et al.*, 1997a). About three-quarters of Swedish dogs have health insurance[1]. Because of the extensive registration and insurance of dogs in Sweden, large amounts of data about demography, health, behaviour, mortality and ancestral background are being stored and made available to breeders and scientists. The databases at the SKC and the insurance company Agria are valuable tools for breeders and breed clubs in selection of breeding stock and in breeding planning. They also offer unique possibilities for both epidemiological and genetic studies on different diseases in dogs.

Screening programmes for different diseases were implemented by the SKC more than 30 years ago. The first programme concerned hip dysplasia (HD), involving centralised evaluation and recording of hip status, assessed by radiographic examination, in young adult dogs. Currently, numerous breeds are also included in screening programmes for other hereditary diseases, such as elbow dysplasia (ED), patellar luxation, heart diseases and eye diseases. Moreover, genetic control programmes based on screening results have been implemented in several breeds, implying mandatory screening of all breeding animals, alone or in combination with the requirement of normal health status.

Despite extensive screening of hip and elbow status and subsequent selection based on the individual's own screening record, i.e., phenotypic selection, the magnitude of improvement has been disappointing. The prevalence of radiographically dysplastic dogs is still high in many breeds, and among the most common causes of euthanasia and costly veterinary care

[1] Ib Ahlén, Agria Insurance Company, personal communication

in numerous large-sized and giant breeds are hip-related problems (Egenvall *et al.,* 2005).

Successful and sustainable breeding of dogs, as well as other animals, requires a well-designed breeding programme. The objective of a breeding programme is genetic improvement of the traits defined in the breeding goal, i.e., the traits one wishes to improve, for the population. Recording of pedigree information, as well as of the traits used as selection criteria to achieve the breeding goal, constitutes the basis of a breeding programme. The recorded traits need to be closely correlated with the breeding goal traits. Applied to joint diseases, this means that the radiographic assessment of hip and elbow status needs to be a good predictor of subsequent clinical problems related to hip and elbow health. The accuracy of using radiographic hip and elbow status in young dogs as indirect selection criterion, aiming at improved clinical hip and elbow health, has been little examined although selection against HD has been based on screening records for decades.

Effective selection is facilitated by the use of appropriate methods for genetic evaluation. Mixed linear models for prediction of breeding values have been used extensively in breeding of livestock for several years (Simm, 2000). However, in dog breeding this methodology has been applied only to a limited extent. Selection of dogs has traditionally been based mainly on the individual's own record.

This thesis aims at investigating the possibilities of more efficient breeding strategies for improved hip and elbow health in Swedish dogs by improving the genetic evaluation of HD and ED, and by evaluating the clinical significance of radiographic hip status.

Background

Some Characteristics of Dog Breeding

The domestic dog (*Canis familiaris*) shows a unique genetic variation, reflected by a large diversity in size, conformation and behaviour. At present, there are more than 350 breeds worldwide recognised by the international canine organisation Fédération Cynologique Internationale (FCI), out of which 329 are recognised by the SKC. Each breed constitutes a relatively closed genetic pool and nearly all breeds were shown to represent genetically distinct populations in the sense that individual dogs could be correctly assigned to breed on the basis of their genotypes, assessed by microsatellite typing (Parker *et al.*, 2004; Ostrander & Wayne, 2005).

Dog breeds have been selected for specific characteristics and behaviours, which not only have led to large diversity between breeds, but also to reduced genetic variation within breeds. The large number of different dog breeds implies breeding in many small populations, commonly originating only from small numbers of founders. In addition, many of the breeds have been subjected to population bottlenecks, popular-sire effects and systematic use of inbreeding (McGreevy & Nicholas, 1999; Karlsson & Lindblad-Toh, 2008). The genetic homogeneity within dog breeds, a consequence of inbreeding, causes problems related to heritable diseases. There are more than 500 heritable diseases reported in dogs (OMIA, 2010) with varying prevalence depending on breed and disease. Some diseases are known to be caused by a single mutation, but most of the heritable diseases are likely to be quantitative and influenced by several genes and environmental factors (OMIA, 2010). The genetic structure of the dog makes it a valuable resource for studying the genetic basis of quantitative traits, as well as a model organism for human diseases (Karlsson *et al.*, 2007; Karlsson & Lindblad-Toh, 2008).

The large variation in disease prevalence and purpose between different dog breeds result in highly breed-dependent breeding goals. As opposed to breeding of livestock, the breeding goals for dogs are not determined by production traits and economic aspects, but instead related to the morphology, health and behaviour of the dog. Many of the relevant characteristics in dog breeding, for example behavioural traits, are difficult to measure objectively and subjective measures are therefore commonly used as basis for genetic evaluation. Traditionally, the main focus is on morphological traits and performance in dog shows in most of the dog breeds (McGreevy & Nicholas, 1999; van Hagen *et al.*, 2004; Liinamo & van Arendonk, 2006). Because the most successful show dogs often are used extensively in breeding, show judges considerably influence the development of many dog breeds (Mäki *et al.*, 2005; Liinamo & van Arendonk, 2006).

Because dog breeding is almost entirely performed as a hobby, individual dog breeders play an important role in the development of dog breeds. The large number of dog breeds, as well as number of breeders involved, means varying interests and breeding goals, creating a diverse basis for genetic evaluation and selection of dogs. However, there are national and international regulations about breeding of dogs. International breeding regulations are prescribed by for example the FCI (Fédération Cynologique Internationale, 2010) and the European Convention for the Protection of Pet Animals (Council of Europe, 1987). In Sweden, general rules and regulations regarding animal welfare, also concerning dog breeding, are governed by the Swedish Board of Agriculture (Jordbruksverket, 2008). At present, about 320 000 dog owners and breeders are members of the SKC and they are obliged to follow the regulations and breeding policy set up by the SKC (Svenska Kennelklubben, 2009).

Breeding for Healthier Dogs in Sweden

The SKC has long kept records of pedigree information and data about demography, health and behaviour of Swedish dogs. This extensive recording, in combination with open registries, is a valuable resource for breeders and breed clubs. In this section of the thesis, some of the initiatives administered by the SKC, aiming at improved health in Swedish dogs are described.

Screening and Control Programmes

More than 30 years ago, the SKC implemented the use of screening programmes for different diseases to improve health in Swedish dogs. The first programmes concerned HD and hereditary eye diseases. More recently, screening programmes for other heritable conditions, such as ED, patellar luxation and heart diseases, have been developed.

The SKC screening programmes include standardised evaluation and central recording of health status in the SKC database (Table 1, level 1). The records are accessible to the public through the SKC web site. All results, negative as well as positive, are submitted from the veterinary clinics to the SKC for recording. Radiographs from hip and elbow screening are centrally evaluated at the SKC by one of four veterinary radiology experts, so-called panelists, contracted by the SKC. This procedure should minimise bias due to pre-selection of results to be recorded in the SKC database. Selective reporting of screening results is known to be a problem in other countries (Mäki, 2004; Stock & Distl, 2010)

Besides voluntary screening of health status, requirements of mandatory screening of all breeding animals have been implemented in many breeds, being referred to as genetic control programmes (Table 1, level 2). In some breeds, breeding restrictions based on the screening record have been introduced, i.e., only dogs with normal health status are accepted for breeding (Table 1, level 3). The genetic control programmes aimed at reducing the prevalence of the disease in question are based on breed-specific needs and are being introduced on request from breed clubs, after approval by the SKC breeding committee. Irrespective of the level of genetic control programme for HD, the SKC breeding committee has stated that mating of dogs both of which are graded as either moderate or severe HD (grade D or E) is not accepted in any breed due to the increased risk of clinical hip-related symptoms in the offspring.

Table 1. *Description of the different levels of screening and control programmes administered by the Swedish Kennel Club (SKC), and the number of breeds (n) connected to each level of the genetic control programmes for hip (HD) and elbow (ED) dysplasia (in the year 2010).*

Level	*n* HD	*n* ED	Requirements
1	All[1]	All[1]	Standardised screening, evaluation and recording of health status (screening is voluntary)
2	82	13	Mandatory screening of health status for all breeding animals (no breeding restrictions following the screening result)
3	50	1	Only dogs with normal health status are accepted for breeding (for HD/ED this means HD grade A or B and ED grade 0)

[1]Results from HD/ED screening are stored in the SKC database for all breeds.

Besides physical health, the SKC has developed genetic control programmes for mental health, implying mandatory participation in a standardised behavioural test, called 'Dog Mentality Assessment' (Svartberg & Forkman, 2002), for all breeding animals of working dog breeds. Moreover, some of the Swedish native breeds have genetic control programmes related to management of genetic variation. For example, limitations on the maximum number of offspring allowed for each male have been introduced in some breeds, to avoid extensive use of popular sires. Furthermore, programmes for out-crossing with individuals from closely related breeds have been developed in some of the Swedish Scent Hound breeds to increase effective population size.

In summary, the genetic control programmes currently administered by the SKC aim at improved physical and mental health, as well as maintained possibilities for a sustainable breeding with respect to genetic variation. So far, genetic control programmes for physical health have been developed only for hereditary diseases with well defined and validated methods for examination and diagnosis.

Molecular Genetic Tools

Recent advances in molecular genetic studies of the dog and the availability of the canine genome sequence and single-nucleotide polymorphism (SNP) arrays have already led to the identification of an increasing number of genes that cause diseases in dogs (Karlsson & Lindblad-Toh, 2008). The development of DNA tests for different mutations makes it possible to accurately predict the genotype of an individual dog with respect to a specific disease. The possibility of identifying carriers of a defective (recessive) allele enables a more subtle management of breeding programmes to decrease the frequency of a particular disease gene without unnecessary reduction of genetic variation due to excluding potential carriers from breeding.

Results from an increasing number of DNA tests for different diseases in dogs (currently eight different diseases) are being stored in the SKC database. Only DNA tests validated for the Swedish population of the breed considered and performed by laboratories acknowledged by the SKC are being recorded. Moreover, the blood sample for the DNA test must be taken by a veterinarian who also confirms the identification of the dog.

Affected dogs, i.e., dogs with two defective alleles, are not accepted for breeding. However, carriers of one defective allele are allowed to be mated with dogs not carrying the defective allele. In some breeds with mandatory

DNA testing for a specific disease, the use of carriers in breeding has been restricted to only one generation; consequently, all offspring resulting from a mating with a carrier have to be DNA tested and those being carriers are banned from breeding[2].

Breed-Specific Breeding Plans

In 2001, the SKC decided that each breed should have their own breeding plan in addition to disease-specific genetic control programmes, taking into account all aspects relevant in the breeding goal for that specific breed. Thus, the breeding plan should consider and prioritise aspects of both physical and mental health, also taking into account the population structure and genetic variation. Breed-specific goals and strategies should be included, constituting an overall plan for the breed to be used as a recommendation for dog breeders to follow. The responsibility for developing these breeding plans was given to the breed clubs, and at present most breed clubs (i.e., close to 300 out of 329) have submitted a breeding plan to the SKC[3]. Most of the remaining breeds are those with very small populations in Sweden.

Hip and Elbow Dysplasia in Dogs

Canine hip and elbow dysplasia are both heritable developmental diseases of the locomotor system. Hip dysplasia was the first developmental joint disease recognised and has become the most widely studied orthopaedic disease in dogs. Elbow dysplasia is used as a common term for various developmental disturbances leading to osteoarthrosis of the elbow joint (International Elbow Working Group, 2001). Both HD and ED are mainly prevalent in large-sized and giant breeds and develop during the stage of rapid growth (Kasström, 1975; Fry & Clark, 1992). The prevalence and clinical significance of HD and ED vary considerably between breeds (Brass, 1989; Corley, 1992; Swenson *et al.*, 1997a; Genevois *et al.*, 2008).

Pathogenesis and Clinical Symptoms

Hip Dysplasia

The term hip dysplasia means abnormal development of the hip joint (Brass, 1989) and was first described in 1935 (Schnelle, 1935). The development of HD is characterised by a loose, ill-fitting coxofemoral articulation causing insufficient stability which permits the femoral head to move out of the

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[2] Helena Rosenberg, the Swedish Kennel Club, personal communication
[3] Karin Drotz, the Swedish Kennel Club, personal communication

acetabular cup, causing subluxation. The instability alters weight bearing, leading to abnormal wearing of certain areas of the joint surfaces causing inflammation and degeneration (Brass, 1989). Several authors have shown that dogs with higher pelvic muscle mass are more likely to have a normal development of hip joints (Riser & Shirer, 1967; Popovitch *et al.*, 1995; Cardinet III *et al.,* 1997). Joint laxity is an early sign of HD and it is generally accepted that joint laxity early in life is an important factor in the development of HD (Henricson *et al.*, 1966; Lust *et al.*, 1993; Kealy *et al.*, 1997; Smith *et al.*, 2001). However, the most obvious phenotypic expressions are malformation and secondary degenerative joint disease, i.e., arthrosis in hip joints (Henricson *et al.*, 1966).

The clinical significance of HD varies widely among breeds and among individual dogs within the same breed. Clinical symptoms of HD include gait abnormalities, difficulties in rising, walking and running, lameness and pelvic limb muscle atrophy with compensatory shoulder muscle hypertrophy (Fry & Clark, 1992). The clinical symptoms vary throughout the life of the dog with more severe symptoms in older dogs because the osteoarthrosis is progressive (Morgan *et al.*, 2000).

The diagnosis of HD can be based on the owner's history of the behaviour of the dog in combination with clinical findings of joint laxity and/or radiographic examination (Morgan *et al.*, 2000). In puppies and pre-adolescent dogs (<6 months) radiographic diagnosis is less informative because of incomplete ossification of the bones. In most breeds, the majority of dogs are examined for HD by routine radiographic screening at minimum 12 months of age, and the evaluation of hip status is normally based on only the radiographic assessment.

Elbow Dysplasia

Elbow dysplasia was first described in 1974 (Olsson, 1974) and includes several different primary lesions, each leading to osteoarthrosis of the elbow joint (IEWG, 2001). The different entities included in the term ED, as defined by the International Elbow Working Group (IEWG), are ununited anconeal process (UAP) of the ulna, fragmented coronoid process (FCP) of the ulna, osteochondritis dissecans (OCD) of the humerus and incongruity of the articular surface (Hazewinkel & Nap, 2009). All of these entities occur in the elbow joint, due to incongruity that interferes with the formation of the articular surfaces, and can occur alone or in combination (Morgan *et al.*, 2000). Elbow dysplasia is mainly prevalent in young, large-sized growing dogs (Hazewinkel & Nap, 2009). However, the prevalence of different entities of ED varies by breed (Hedhammar & Malm, 2008). In

Rottweilers, the most common entity is FCP (Grøndalen, 1982), whereas OCD is rarely found (Grøndalen, 1979). Bernese Mountain Dogs are also most often affected by FCP (Wind, 1982; Klingeborn, 1986) whereas German Shepherd Dogs are known to have a high prevalence of UAP (Corley *et al.*, 1968).

Clinical symptoms of ED include stiffness in the forelimbs, abnormal movements, lameness and pain in the elbow joint (Grøndalen, 1979). Usually, the specific entity of ED cannot be distinguished by the clinical symptoms (Morgan *et al.*, 2000). The symptoms commonly become apparent early in life, at the age of 4 to 6 months, and often cause faster development of severe arthrosis than HD because most weight is carried on the front legs (Bedford, 1994; Morgan *et al.*, 2000; Mäki, 2004). Many of the worst affected dogs have surgical treatment already before they reach the age of screening (i.e., before 12 months of age) (Hedhammar & Malm, 2008). The heavy load on the elbow joints implies that also mild ED often causes lameness (Mäki, 2004). With time, the clinical symptoms become more chronic and prominent as the development of osteoarthrosis progresses (Morgan *et al.*, 2000).

In clinically affected dogs, the history and clinical symptoms are often suggestive of ED, and the diagnosis is confirmed radiographically by the presence of secondary osteoarthrosis (Bedford, 1994). However, in most dogs, ED is routinely diagnosed by only radiographic assessment performed at the same time as routine hip screening, at minimum 12 months of age.

Radiographic Assessment

Radiographic assessment is widely used for routine evaluation of hip and elbow status, but the methods vary somewhat among different countries and organisations. Internationally, there are three different grading procedures extensively used for radiographic assessment of HD. Hip grading in the United States and Canada is done according to the Orthopedic Foundation for Animals. In the United Kingdom, Ireland, Australia and New Zealand the hip scoring scheme of the British Veterinary Association/the Kennel Club is used. In the rest of Europe, the grading protocol developed by the FCI is the most commonly used (Hedhammar, 2007). For ED grading, the protocol of the International Elbow Working Group (IEWG, 2001) is used in most countries, including Sweden.

Based on the radiograph, hip and elbow joints are graded as either normal or dysplastic. Usually, also the degree of dysplasia is assessed according to severity. The grading of hip and elbow status using discrete categories implies that these traits are so-called ordered categorical traits. In the following section, the grading procedures for HD and ED used in Sweden are described.

Grading of HD in Sweden

Since 2000, the FCI protocol has been used in Sweden (Fédération Cynologique Internationale, 2009). In the radiographic evaluation, the shape of the femoral head and the acetabulum, the joint space and the acetabular angle according to Norberg (i.e., the Norberg angle) are considered, as well as the presence and extent of secondary arthrosis. Hip joints are scored in five categories from A to E, where A and B correspond to two different scoring levels of normal (non-dysplastic) hip joints. The grades C, D and E represent mild, moderate and severe dysplasia, respectively (*Figure 1*).

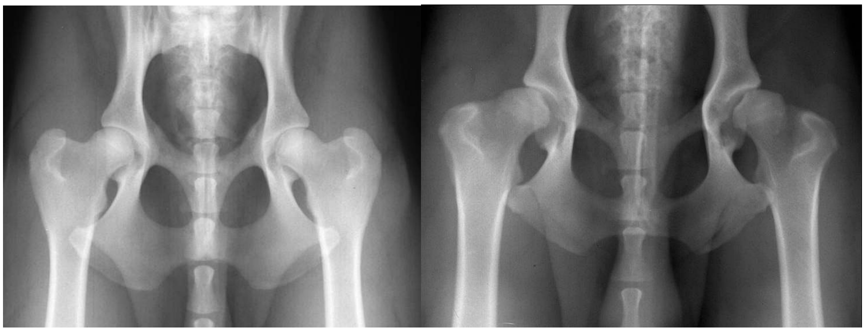

Figure 1. Radiographs of hip joints graded as normal (A) (left) and severe dysplasia (E) (right) (pictures provided by Håkan Kasström).

Before 2000, a slightly modified FCI protocol was used in Sweden, classifying hip joint conformation as "Normal", "Grade I" (slight dysplasia), "Grade II" (moderate dysplasia), "Grade III" (severe dysplasia) or "Grade IV" (very severe dysplasia). This system was a modification of that originally suggested by Schnelle (1954). Severity of osteophyte formation and osteoarthritic deformation were graded separately with the intention not to influence the evaluation of joint conformation (Swenson *et al.*, 1997a). In both current and earlier systems, the grade assigned is based on the worst of the two joints, resulting in only one grade being published for each dog.

Hip joints are radiographed with the dog positioned on its back with the hind legs extended. Since 1991, anaesthesia or sedation during screening is mandatory, according to the FCI protocol (Anonymous, 1992). This facilitates proper positioning by relaxation of the skeletal muscles and favours the detection of joint laxity (Brass, 1989). It also reduces unnecessary exposure to radiation for both dogs and personnel. Since 2004, the type of chemical restraint used for sedation has been recorded in the protocol for each dog. For an official record of hip status in the SKC registry, the dog should be at least 12 months old (18 months in some giant breeds) and should have an identification number (tattoo or microchip).

Grading of ED in Sweden

Official grading of ED in Sweden follows the guidelines of the International Elbow Working Group (IEWG, 2001). Grading of ED is based on the degree of arthrosis present, divided into four classes from normal (Grade 0) to severe arthrosis (Grade III), based on the size of osteophytes present in the joint (*Figure 2*). Osteophytes of less than 2 mm are graded as mild arthrosis (Grade I), osteophytes between 2 and 5 mm are graded as moderate arthrosis (Grade II) and osteophytes over 5 mm are graded as severe arthrosis (Grade III) (Audell, 1990).

Figure 2. Radiographs of elbow joints graded as normal (Grade 0) (left) and severe arthrosis (Grade III) (right) (pictures provided by Håkan Kasström).

Elbow joints are radiographed in a lateral position with the joint fully flexed. Elbow screening is usually performed at the same time as hip screening, and the minimum age for an official registration of elbow status in the SKC is 12 months.

Genetic Background

Both HD and ED are recognised as quantitative traits (e.g., Swenson *et al.*, 1997a; Swenson *et al.*, 1997b). HD was reported as a heritable trait already in the 1950's (Schales, 1956), and an inherited disposition of ED was indicated in several studies during the 1980's (Grøndalen, 1982; Wind, 1986). Heritabilities for both these diseases have been estimated in several dog populations and the estimates range from 0.20 to 0.60 for HD (Henricson *et al.*, 1972; Hedhammar *et al.*, 1979; Swenson *et al.*, 1997a; Mäki *et al.*, 2000) and from 0.10 to 0.77 for ED (Guthrie & Pidduck, 1990; Grøndalen & Lingaas, 1991; Swenson *et al.*, 1997b; Mäki *et al.*, 2000). Despite the variability in estimates of heritability, the results clearly indicate that both HD and ED are diseases that can be reduced by selection.

Many categorical traits are assumed to be under polygenic control. Thus, the trait is assumed to have an underlying normally distributed continuous variable (often called the liability) (Falconer & Mackay, 1996). The quantitative and categorical nature of HD and ED means that the phenotype is not the most accurate indicator of the genotype because the individual's phenotype on the underlying scale based on its hip or elbow status is imprecisely known. Nevertheless, the severity of HD and ED in the parents was shown to be related to the percentage of dysplastic offspring as well as the severity of dysplasia in the offspring (Henricson *et al.*, 1966; Henricson *et al.*, 1972; Hedhammar *et al.*, 1979; Swenson *et al.*, 1997a; Swenson *et al.*, 1997b).

The existence of major genes influencing HD has been suggested by several authors (Mäki *et al.*, 2004; Janutta *et al.*, 2006a). Studies aimed at finding regions in the dog genome that contain genes contributing to HD indicate that several canine chromosomes harbour putative quantitative trait loci (QTLs) involved in the expression of HD (Chase *et al.*, 2004; Todhunter *et al.*, 2005; Marschall & Distl, 2007). Moreover, FCP, one of the entities included in ED, has been suggested to be controlled by a major gene (Everts, 2000). However, no causative genes for FCP have yet been found (Temwichitr *et al.*, 2010).

Environmental Factors

In addition to the genetic influences, the phenotypic expressions of HD and ED are affected by various non-genetic factors. Several studies have shown that limited food intake and slow rate of body growth beneficially affect the development of hip and elbow joints in growing and adolescent dogs (Riser *et al.*, 1964; Kasström, 1975; Hayes *et al.,* 1979; Kealy *et al.*, 1992; Kealy *et al.*, 1997; Sallander *et al.*, 2006). Moreover, other studies have focussed on the effects of systematic environmental factors, such as sex, age at screening, birth month and year of screening, on the radiographic assessment of hip and elbow joints (e.g., Guthrie & Pidduck, 1990; Grondalen & Lingaas, 1991; Swenson *et al.*, 1997a; Swenson *et al.*, 1997b; Leppänen *et al.*, 2000a; Mäki *et al.*, 2000; Janutta *et al.,* 2006b). Also factors related to the procedure of screening and evaluation of hip and elbow joints (e.g., veterinary clinic, anaesthesia and panelist) have been suggested to affect the radiographic assessment of joint status in other countries (Schnepf, 1976; Madsen & Svalastoga, 1991; Köppel & Lorinson, 1994; Mäki *et al.*, 2000).

Selection for Hip and Elbow Health

Current Practice and Its Limitations

In the current selection for improved hip and elbow health of dogs in Sweden, as well as in most other countries, the individual's own screening record is used as selection criterion, with subsequent phenotypic selection (i.e., mass selection). In many breeds, only dogs with normal hip status (A or B) are accepted for breeding (Table 1) and the use of dysplastic dogs in breeding is unusual in most breeds in Sweden.

Despite efforts to reduce the frequency of HD and ED by means of genetic control programmes, the reduction has been disappointing in several breeds. Low or no improvement in HD following phenotypic selection has been reported in several countries (e.g., Lingaas & Heim, 1987; Willis, 1997; Leppänen & Saloniemi, 1999).

The limited success of breeding programmes against HD and ED is most likely caused by several factors. In some breeds, lack of genetic progress may be partly explained by the extent to which breeders prioritise joint diseases in selection, in relation to other traits in the breeding goal (McGreevy & Nicholas, 1999; Mäki *et al.*, 2005). Moreover, unfavourable genetic correlations between HD/ED and other traits selected for (e.g., behavioural and morphological traits) may exist and thus make selection less efficient. However, studies of correlations (genetic and phenotypic) between joint status and other traits are scarce (Mackenzie *et al.*, 1985; Liinamo & van Arendonk, 2006; Roberts & McGreevy, 2010).

Furthermore, the categorical nature of HD and ED makes phenotypic selection less efficient than for continuous traits because the individual's phenotype on the liability scale is imprecisely known from its hip or elbow status. Not being able to discriminate between individuals with high and low liabilities within the same phenotypic category implies that all dogs with the same hip or elbow status are put into only one category even though their liabilities may differ. The selected individuals are therefore a random sample from the desired category, with the expected mean of the selected dogs being equal to the mean of all dogs in that category. The selection differential depends on the incidence of the trait, being largest when the proportion of healthy dogs equals the proportion to be selected (Falconer & Mackay, 1996). Thus, in breeds where the proportion of dogs graded as normal hip or elbow status is much larger than the proportion of dogs selected for breeding, selection based on only the individual's phenotypic record becomes inefficient.

The phenotypic record is influenced also by non-genetic factors; consequently, the phenotype is not the most accurate indicator of the genotype. This makes the genetic evaluation based on radiographic hip and elbow status imprecise, limiting the genetic progress in HD and ED. For example, differences between veterinary clinics with respect to chemical restraint used for sedation during hip and elbow screening have caused concern and debate among dog breeders in Sweden, due to indications of heavier sedation causing worse hip status as a result of increased joint laxity.

Screening Results as Selection Criterion

The main purpose of the genetic control programmes for HD and ED is to use the screening records as indirect selection criteria for improved hip and elbow health. However, the screening results are also being used as an early predictor of clinical problems related to HD and ED. As stated in the introduction, the trait recorded as basis for genetic evaluation needs to be closely correlated with the breeding goal trait for the breeding programme to be efficient. For many years, genetic evaluation of HD and ED has been based on radiographic assessment of hip and elbow status worldwide (Hedhammar, 2007; Hedhammar & Malm, 2008). Despite this, investigations of the association between radiograpically assessed hip/elbow status and subsequent clinical symptoms are lacking. The accuracy of using radiographic hip and elbow status in young dogs as basis for selection aimed at improved clinical hip and elbow health has not been quantified.

Prospects for Improved Genetic Evaluation

Genetic evaluation including the phenotypes of relatives, in addition to the individual's own screening record, would more accurately estimate the genotype for HD/ED. This information can be accounted for by using mixed linear models to predict breeding values (EBVs) for HD and ED, which also allows for simultaneous adjustment for systematic environmental factors. Prediction of breeding values for HD and ED using Best Linear Unbiased Prediction (BLUP) has been suggested in several studies (e.g., Lingaas & Klemetsdal, 1990; Willis, 1997; Leppänen & Saloniemi, 1999; Hou *et al.*, 2010). Nevertheless, in practical dog breeding this methodology has been used only to a limited extent, recently being introduced for HD in some countries (e.g., Finland, Norway and Germany) (Mäki, 2004; Stock & Distl, 2010). However, in countries where BLUP breeding values are available, breeding restrictions are commonly still based on the phenotypic record for HD and not on the predicted breeding value (Stock & Distl, 2010) [4].

Studies of the potential or realised genetic responses in HD or ED using BLUP instead of phenotypic selection are scarce (Leighton, 1997; Stock & Distl, 2010) probably because of the limited use of BLUP for HD and ED in practice. Thus, it is not known to which extent the use of BLUP for improvement of categorically scored hip and elbow status can be expected to increase selection efficiency, or what impact BLUP will have on inbreeding levels.

[4] Katariina Mäki, the Nordic Kennel Union/the EBV Group, personal communication

Aims of the Thesis

The overall hypothesis of this thesis was that a more effective breeding programme for improved hip and elbow health in Swedish dogs could be achieved by applying enhanced methodology that uses available information more efficiently. The specific aims were to:

- Assess the importance of genetic and environmental factors influencing radiographic assessment of HD and ED
- Evaluate the association between radiographic assessment of hip status and subsequent incidence of clinical problems and mortality related to the hip joint
- Develop a statistical model for prediction of breeding values for HD and ED based on radiographic appearance
- Compare selection based on phenotypic records and BLUP breeding values for improved hip status.

Summary of the Investigations

Materials

Hip and elbow health in Swedish dogs was studied by combining data from different sources. In this section a condensed description of materials studied in Paper I to IV is given.

In Paper I-III, data on screening results for HD and/or ED from the SKC database were used together with data from a questionnaire (Paper I) and insurance data (Paper II). In addition to information on hip and elbow status, SKC data included registration number and pedigree information, date of birth, date of screening, sex of the dog, veterinary clinic and panelist. SKC data for Paper I also included annotations of hip-joint laxity. Paper IV was based on simulated data.

The selection of breeds differed somewhat between the papers (Paper I-III) depending on the objective of the study. However, all breeds studied were included in a genetic control programme for HD in the SKC, implying mandatory hip screening of all breeding animals. The breeds were selected based on the proportion and number of dogs screened for and affected by HD and ED.

Integration of Questionnaire Data and SKC Data

Paper I was based on a questionnaire, sent to all veterinary clinics performing official radiographic screening of hip and elbow joints, to increase the knowledge of routines for hip and elbow screening in Sweden. To study the impact of sedation method on the screening result for HD and ED, questionnaire data on sedation methods were merged with SKC data including information on hip and elbow status for eight breeds of dogs, screened during a period from January 2002 to March 2003. The breeds included were Bernese Mountain Dog (BMD), Boxer, German Shepherd

Dog (GSD), Golden Retriever (GR), Labrador Retriever (LR), Newfoundland, Rottweiler (RW) and Saint Bernard. By using information about veterinary clinic in the SKC data, the screening result for each dog was combined with information from the questionnaire about sedation method used at each veterinary clinic. Clinics that claimed to make deviations from the normal sedation routine in more than 10% of the cases were excluded from the analyses to minimise the risk of misclassification. As a result, 174 clinics were included in the study. In total, 5877 dogs examined for HD and 5406 dogs examined for ED were included.

Integration of Insurance Data and SKC Data

To evaluate the association between radiographic assessment of hip status and reported incidence of hip-related veterinary care and mortality (Paper II), insurance data from Agria were merged with SKC data, based on the registration number of the dog. Variables in Agria data used for this study were identification and registration number of the dog, breed, sex, date of birth, information on whether the dog was covered for life and/or veterinary care, dates of enrolment in and ending of insurance, dates of life and/or veterinary claim and diagnostic codes. Dogs of five breeds (BMD, GSD, GR, LR and RW) screened during 1995-2004 and covered by an insurance plan for veterinary care or life, at the time of screening, were included. The study populations included between 1667 and 10 663 dogs per breed.

SKC Data for Genetic Analyses of HD and ED

In Paper III, SKC data were used to estimate genetic parameters and genetic trends for HD and ED in two breeds: BMD and RW. Data included results of hip status for 14 693 RW and 8221 BMD and elbow status for 11 891 RW and 7963 BMD. Most of the recorded data were for dogs born in the years 1984-2001. However, for RW data on HD were available already from the beginning of the 1970's. Pedigree information for each breed consisted of animals with records for HD and/or ED and their ancestors, comprising 16 614 RW and 9835 BMD.

Simulated Data

In Paper IV, simulated data were used to compare improvement of categorically scored hip status based on truncation selection on phenotypic records versus BLUP breeding values. To resemble the situation in various real dog breeds, four different populations with respect to initial prevalence of HD and population size were modelled. For each factor, two levels corresponding to contrasting values of the concerned parameter were defined, resulting in four main scenarios. In addition, alternative scenarios with respect to proportion of dogs with a screening record for HD, genetic correlation, selection method and selection rules were evaluated, with reference to one or some of the main scenarios.

Methods

In this section a condensed description of methods applied in Paper I to IV is given.

Estimation of Systematic Environmental Effects

The impact of different systematic environmental factors on the screening result for HD and ED were estimated in Paper I and III. The effects studied were sedation method (Paper I), veterinary clinic (Paper I), sex (Paper I and III), age at screening (Paper I and III), breed (Paper I), birth month (Paper III), panelist (Paper III), year of examination (Paper III) and a combined random effect of veterinary clinic and year of examination (Paper III).

In Paper I, logistic regression with procedure Logistic (SAS, 1999) was used to examine the impact of sedation method on HD and ED as the factor of main interest. The effects of sex, breed, age at screening, veterinary clinic (nested within sedation method) and all two-way interactions between main effects were offered for inclusion in the model. Two approaches were tested: an ordered logistic regression using a cumulative-logit link function with a proportional-odds model applied to the ordinal responses 1-5 and 1-4 for HD and ED, respectively, and a logistic regression using dichotomous responses with a logit link function. However, the score test of the proportional odds assumption was significant for both HD and ED, indicating that this assumption did not hold. Therefore, only results from the dichotomous logistic regression were presented.

For dogs with HD (grade C, D or E), the effect of sedation method, breed and age at screening on hip-joint laxity was studied in an additional model using dichotomous logistic regression.

In preliminary analyses for Paper III, the impact of systematic environmental effects on HD and ED was examined using analysis of variance with procedure Mixed (SAS, 1999).

Survival Analysis of Mortality and Veterinary care

To quantify the impact of radiographic hip status on time from hip screening to first HD-related veterinary claim and mortality (life claim) in

Paper II, breed-specific multivariable Cox proportional-hazards models were used. In addition, the effects of sex, birth season and a time-varying covariate of year were studied in each breed. Three separate Cox models were fitted to analyse time to early life claim (within 200 days after screening), time to late life claim (later than 200 days after screening) and time to first veterinary claim.

Additional analyses, for the five breeds combined, were done to investigate the effects of hip status, breed and the interaction between hip status and breed, using similar models of time to early versus late life claim and time to first veterinary claim. The statistical software package Stata/IC 10.0 (Stata, 2008) was used for all survival analyses.

Estimation of (Co)variance Components and Breeding Values

Variance components and breeding values for HD and ED were estimated in Paper III, using a univariate mixed linear animal model including the fixed effects of sex, birth month, age at screening and year of examination, the combined random effect of veterinary clinic and year of examination and the random effect of animal. Bivariate analyses were used to estimate the genetic correlation between HD and ED in each breed (RW and BMD). In addition, an extended univariate model, also including genetic group effects, was used to predict breeding values accounting for the genetic level of the various subpopulations. Genetic groups were defined for animals with unknown parents in the pedigree, based on the year of birth and the origin of the animal. The DMU software (Madsen & Jensen, 2000) was used to estimate genetic parameters by a restricted maximum likelihood approach and to predict BLUP breeding values.

Because data from two different HD grading systems (the old Swedish system used until 1999 and the FCI system) were included in the analyses, transformation of HD grades to a common scale was done prior to the analyses. Transformation was done also for ED to account for the possibility of unequal differences between scores. The grades were transformed by calculating the expected value of the underlying variable for each grade, assuming normally distributed variables.

Stochastic Simulation of Selection Strategies

For each scenario defined in Paper IV, two alternative selection strategies for improved hip status were compared: phenotypic selection and BLUP selection. Moreover, optimum contribution selection (OCS) based on BLUP was compared with truncation selection on BLUP for one of the scenarios.

Hip dysplasia was defined as a categorical trait with five classes and a heritability of 0.45 on the liability scale. Besides HD, selection for a continuous trait with heritability of 0.25 was simulated to represent selection for other traits included in the breeding goals for dogs. An additive mode of inheritance was assumed and the economic weights for both traits were set to unity. The genetic correlation between the traits was set to zero in all main scenarios. Furthermore, genetic correlations of -0.3 and -0.6 were modelled for one of the main scenarios.

Alternative scenarios, only allowing dogs graded as A or B in breeding, were simulated for two of the main scenarios to evaluate the effect of stricter phenotypic selection on genetic progress. Furthermore, phenotypic selection without any distinction between A and B dogs, in addition to excluding C dogs, was simulated.

A mixed linear animal model was used to predict BLUP breeding values with the DMU software (Madsen & Jensen, 2000). OCS was performed using the EVA software (Berg *et al.*, 2010). The scenarios were modelled over a period of 25 years using stochastic simulation with the software package ADAM (Pedersen *et al.*, 2009). Each scenario was replicated 50 times. The genetic response, inbreeding rate and frequency distribution of the categories for HD were followed annually for all scenarios.

Main Findings

Impact of Sedation Method

In Paper I it was shown that sedation method significantly affected the screening result for HD. Use of acepromazine (Plegicil® vet.; Pharmaxim Sweden AB) for sedation gave less than half the odds of HD, compared with the more commonly used methods, medetomidine and butorphanol (Domitor® vet.; Orion and Torbugesic-SA®; Wyeth) or medetomidine alone. Moreover, in the analysis of hip-joint laxity, acepromazine gave one-fifth the odds of joint laxity compared with use of medetomidine and butorphanol, given that the dog was dysplastic.

The probable explanation of these findings is that acepromazine gives a less heavy sedation than medetomidine and butorphanol or medetomidine alone. It has been suggested that the use of anaesthesia or sedation relaxes the muscles so that a masked joint laxity might be more easily detected (Bardens, 1972; Morgan & Stephens, 1985; Corley, 1989). In a study comparing FCI hip grading between anaesthetised dogs and non-sedated non-anaesthetised dogs, the prevalence of HD and the rate of hip-joint laxity were shown to be significantly higher in anaesthetised dogs (Genevois *et al.*, 2006). Our results add support to the hypothesis that a more heavy sedation is associated with an increased degree of hip-joint laxity, and an increase in the HD observed by radiographic screening.

The significant effect of sedation method on radiographic hip status implies that the individual's screening result for HD alone imprecisely estimates its breeding value, and is therefore not the most accurate basis for selection.

Impact of Other Systematic Environmental Factors

In addition to sedation method, several other factors were shown to significantly affect the radiographic assessment of HD and ED. A significantly higher prevalence of HD was found in females than in males. Conversely, for ED the prevalence was found to be highest in males (Paper I and III). Moreover, a significant effect of age at screening on hip and elbow status was shown, implying increased prevalence of HD and ED with age (Paper I and III). Similar effects of sex and age on hip and elbow status have been reported in several studies (Guthrie & Pidduck, 1990; Distl *et al.*, 1991; Grondalen & Lingaas, 1991; Swenson *et al.*, 1997a; Beuing *et al.*, 2000; Leppänen *et al.*, 2000b; Wood & Lakhani, 2003). A sex-related difference in the prevalence of HD could be explained by an effect of secondary sex characteristics, for instance differences in growth rate or sex hormones (Swenson *et al.*, 1997a). An unfavourable effect of age on hip and elbow status was expected as osteoarthritic changes are expected to worsen with age.

The effect of year of examination was significant for both HD and ED, showing an unfavourable trend (Paper III). This indicates that the routines for management of the dogs (e.g., feeding and exercise practices) and/or the procedures for screening and evaluation of hip and elbow status have changed over time. Possible explanations could be changes in sedation routines towards using more heavy sedation and changes in the grading system (e.g., in the year 2000 the old Swedish system for grading of HD was replaced by the FCI system). An unfavourable trend for the effect of birth year on HD and ED was found in earlier studies (Leppänen *et al.*, 2000a; Mäki *et al.*, 2000).

The interpretation of the effect of birth month was not straightforward. For HD there was a tendency towards better hip status for dogs born during the first two quarters. For ED, no uniform trend was visible (Paper III). Leppänen *et al.* (2000a) found a similar effect of birth month on HD, with dogs born during February-July having better hip status. The suggested explanation for this trend was that puppies born in spring or summer had more opportunity for outdoor exercise than puppies born in autumn and winter, which may positively affect skeletal development. For ED, Janutta *et al.* (2006b) showed that dogs born between April and June had better elbow status than dogs born in other months of the year, which is consistent with the above explanation.

Association between Radiographic Hip Status and Clinical Problems

The effect of radiographic hip status was highly significant for both veterinary care and mortality related to HD in all of the breed-specific analyses, as well as in the analyses including all five breeds together, indicating a strong association between the screening result for hip status and subsequent incidence of clinical problems related to HD (Paper II). The hazard ratio increased with deteriorating hip status, indicating a shorter time to event. Dogs with moderate or severe dysplasia (D or E) at screening had markedly increased hazards of life and veterinary claims related to HD, compared with dogs assessed as free or mild. However, the difference in survival between dogs graded as free (A or B) or mild (C) at screening was small for both life and veterinary claims.

The effect of breed was significant for all models in the across-breed analyses. The GSD had the highest hazard ratio whereas GR and LR had the lowest hazard ratio for all models. The interaction between hip status and breed was not significant in any model, implying that the effect of hip status on time to veterinary care and mortality related to HD was the same irrespective of breed.

The strong association between radiographically assessed hip status and subsequent incidence of hip-related veterinary care and mortality suggests that hip screening records can be used for selection in breeding against clinical problems related to the hip joint. However, the usefulness of hip screening as a diagnostic tool for predicting clinical problems in individual dogs was found to be unsatisfactory and breed-dependent. For example, the probability of a veterinary claim related to HD within eight years from screening for a GSD with severe HD was 48% and for an LR the corresponding probability was only 18%.

Genetic Parameters and Genetic Trends

The genetic analyses of HD and ED in Paper III showed that there was considerable genetic variation in both traits in Swedish RW and BMD. The heritability estimates for HD and ED were similar in RW and BMD (0.38 and 0.42 for HD; 0.34 and 0.38 for ED). The estimated genetic correlation between HD and ED was weak and positive for RW ($r_g = 0.23 \pm 0.05$) and not different from zero for BMD (r_g = 0.06 ± 0.06) indicating that selection against HD could not be expected to reduce the prevalence of ED to any considerable extent, and vice versa.

The effect of genetic groups was not significant and the estimates of the genetic group effects were generally small, suggesting that genetic groups were not needed in the model for prediction of breeding values.

Genetic trends for HD and ED were favourable in both breeds, indicating a genetic improvement corresponding to 0.57-0.67 genetic standard deviation units during the last 10-year period, depending on breed and trait (*Figure 3* and *4*). Despite the favourable genetic trends, the improvement in HD was not reflected in the phenotypic trend, illustrated as the proportion of dogs graded as normal (A or B) each year (*Figure 3*). This is probably to some extent due to the unfavourable trend for year of examination (Paper III).

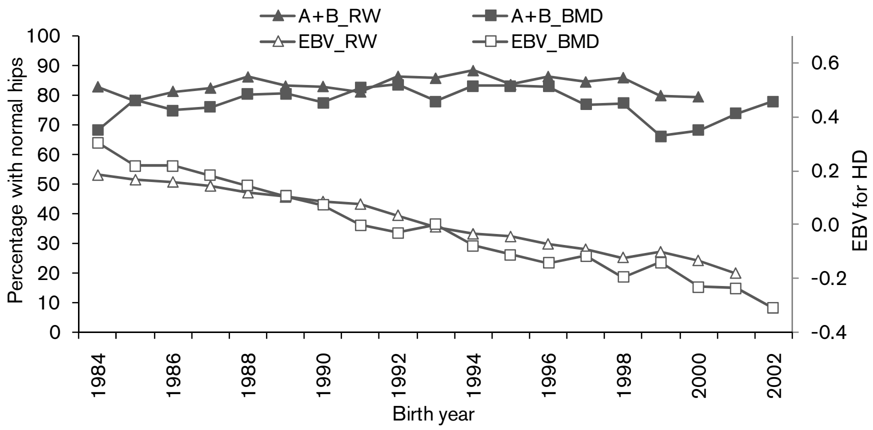

Figure 3. Percentage of Rottweilers (RW) and Bernese Mountain Dogs (BMD) graded as normal hip status (A or B) (solid symbols) and predicted breeding values (EBVs) for hip dysplasia (HD) in RW and BMD (open symbols), by birth year (Paper III).

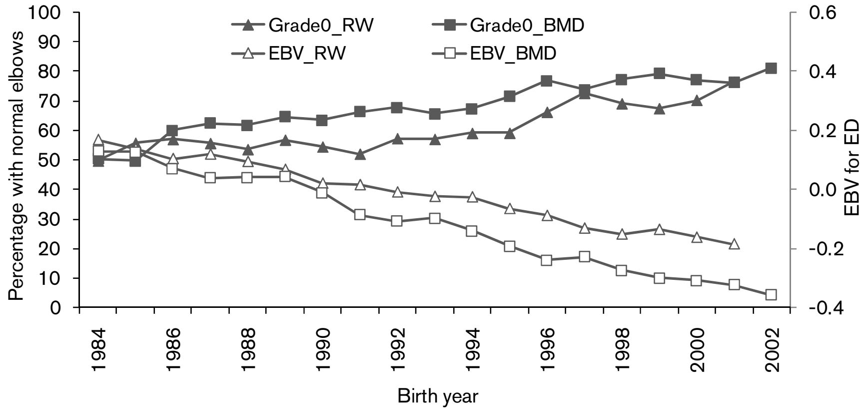

Figure 4. Percentage of Rottweilers (RW) and Bernese Mountain Dogs (BMD) graded as normal elbow status (grade 0) (solid symbols) and predicted breeding values (EBVs) for elbow dysplasia (ED) in RW and BMD (open symbols), by birth year (Paper III).

Evaluation of Selection Strategies

In all scenarios studied, the genetic change for HD was larger when using BLUP selection compared with phenotypic selection. The average yearly genetic gain for HD (over year 6-25) was 1.2 to 1.5 times larger using BLUP instead of phenotypic selection. Because the BLUP model did not include any fixed effects, the differences between BLUP selection and phenotypic selection found in this study are most likely underestimated, showing the minimum expected benefit of using BLUP selection.

The benefit of BLUP was also reflected in a faster reduction of HD prevalence using BLUP breeding values compared with phenotypic records in all scenarios. The difference between selection strategies, with respect to change in HD prevalence, was larger at high initial prevalence of HD (*Figure 5*).

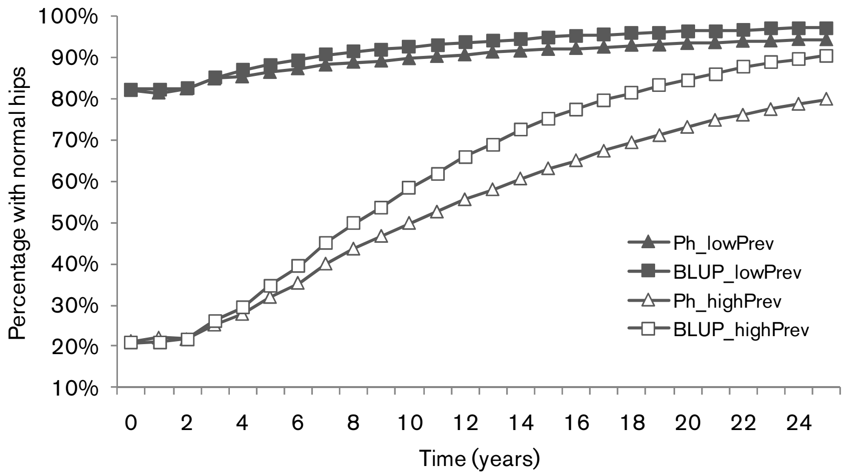

Figure 5. Phenotypic trend illustrating the percentage of dogs graded as normal hip status (A or B), using phenotypic (Ph) selection versus BLUP selection, in a simulated population with low (solid symbols) and high (open symbols) initial prevalence (Prev) of hip dysplasia (HD), respectively (Paper IV).

The average rate of inbreeding per generation was higher when using BLUP compared with phenotypic selection in all scenarios, in the small population being higher than what is normally recommended. However, by using OCS in the small population, both the rate and onset of inbreeding was lowered to approximately the same level as for phenotypic selection, but with a considerably higher genetic gain than achieved with phenotypic selection.

The benefit of BLUP selection over phenotypic selection was irrespective of initial HD prevalence, population size and proportion of dogs with a screening record. This indicates that BLUP selection can be expected to be effective in breeds with different population structures and prevalence of HD. Moreover, the benefit of BLUP found in this study, for a trait mimicking HD, is likely to apply for other quantitative diseases in dogs, such as ED, which are measured as categorical traits with similar heritability.

Stricter phenotypic selection, only allowing dogs with normal hip status (A or B) in breeding, caused reduced overall genetic progress and only marginally higher genetic progress for HD, compared with when dogs with mild dysplasia (grade C) were allowed in breeding. By treating A and B dogs the same in the phenotypic selection, in addition to excluding C dogs, the genetic progress for HD was considerably lowered.

General Discussion

Screening programmes in combination with subsequent phenotypic selection for improved hip and elbow status in dogs have been used in several countries for many years. Despite this, HD and ED are still among the most common diseases in many breeds, causing pain, loss of function and preterm euthanasia in dogs, as well as economic and emotional impacts on dog breeders and owners.

An efficient breeding programme requires that the trait used as the basis for selection is accurately measured and closely correlated with the trait of interest. Furthermore, genetic evaluation and selection should be based on appropriate methods to use the available information efficiently.

The results presented in this thesis support the use of screening results for hip status in selection aimed at reduced risk of clinical problems related to HD based on the following findings: 1) Radiographic hip status was found to be strongly associated with the incidence of veterinary care and mortality related to HD (Paper II); 2) radiographic assessment of hip status showed considerable genetic variation and moderate heritability (Paper III). Nevertheless, the results indicate that the individual's own screening result alone may not be the most accurate basis for selection because the radiographic assessment of both hip and elbow status is affected by several environmental factors, for example the method of sedation used (Paper I and III).

Prediction of breeding values based on screening records for HD and ED using BLUP makes it possible to include all available information about hip or elbow status in relatives, and simultaneously adjust for systematic environmental effects. Selection based on BLUP breeding values was shown to enable a more efficient selection (Paper III and IV) compared with selection based on phenotypic records alone. Hence, by using BLUP selection instead of phenotypic selection, a faster genetic gain and accordingly a more rapid reduction in dogs graded as dysplastic could be expected (Paper IV). Moreover, the genetic trend based on EBVs, as opposed to the phenotypic trend, makes it possible to more accurately monitor the genetic change (Paper III).

Based on the results in this thesis, it is suggested to implement breeding value prediction for HD and ED using BLUP to enable a more accurate genetic evaluation and a faster genetic progress. However, because BLUP selection most likely will result in higher rates of inbreeding compared with phenotypic selection (Paper IV), the use of BLUP in practical breeding should be combined with tools to monitor and control the rate of inbreeding. Optimum contribution selection is the best tool in theory, but requires adaptation before being implemented in practical dog breeding.

The use of screening records as selection criterion, the statistical model for breeding value prediction and practical implications related to introduction of EBVs for HD and ED are discussed in more detail below. Furthermore, some issues related to optimisation of breeding strategies and to the overall breeding programme are discussed.

Selection Criteria versus Breeding Goal Traits

A strong phenotypic association between radiographic hip status and subsequent clinical problems related to HD was found in Paper II. However, for the screening record to be a good criterion for indirect selection on the breeding goal trait, i.e., clinical hip or elbow health, there also needs to be a high genetic correlation between radiographic hip status and clinical problems. Several studies have shown that the phenotypic and genetic correlation estimates in many situations are highly correlated, indicating that the phenotypic correlation is a good estimate of the genetic correlation (Koots & Gibson, 1994; Roff, 1995). Thus, it is plausible that the strong phenotypic association found between radiographic hip status and subsequent hip-related clinical problems in our study implies a high genetic correlation, although this remains to be confirmed. Moreover, the genetic and phenotypic correlations between the screening record for ED and clinical problems related to the elbow joint remains to be investigated. However, analyses of genetic correlations would probably require larger data sets than those available for our study (Paper II).

Despite both HD and ED being developmental diseases of the locomotor system with similar heritability, there are some differences between the traits worth mentioning in relation to the use of screening results as indirect selection criterion. ED usually has an earlier onset of clinical problems compared with HD (Morgan *et al*., 2000). Early onset of a disease normally facilitates selection; however, for ED the early onset also implies that some dogs with severe clinical problems at a young age get operated before 12 months of age (Hedhammar & Malm, 2008). These dogs will not get an official screening record for ED in the SKC database, or in the worst case they will be graded as normal at a later official screening. It would be necessary to include accurate information about elbow status of dogs operated before official screening in the genetic evaluation to get unbiased breeding values for these individuals and their relatives. Furthermore, ED (measured as the amount of secondary arthrosis in the joint) can be due to different primary lesions, with varying prevalence between breeds. Thus the genetic correlations between ED and other traits in the breeding goal are likely to be breed-specific. Moreover, the genetic correlation between the screening result for ED and the breeding goal trait can be expected to differ between breeds to a larger extent than for HD.

Specification of the Statistical Model

Linear versus Non-Linear Models

The use of EBVs for HD and ED in practice requires an accurate statistical model, suited for the structure of the pedigree information and data available. Moreover, the model should be computationally feasible and meet the demands of the users. Because HD and ED are categorical traits, it could be argued that a threshold model is preferable to a linear model because it accounts for the distribution of data. However, the largest benefit of a threshold model can be expected for a dichotomous (0/1) trait with uneven frequency distribution (Meijering & Gianola, 1985). HD and ED are measured in five and four classes, respectively. Abdel-Azim & Berger (1999) showed in a simulation study that the use of several categories and large data sets with good pedigree structure reduces the benefit of a threshold model. The population structure in their study resembled that in dairy cattle, and it therefore needs to be confirmed whether the conclusions hold for dog populations.

In most studies of genetic parameters for HD and ED, linear models have been used. In a study by Silvestre *et al.* (2007), based on 313 Estrela Mountain Dogs, estimates of genetic parameters, genetic trends and ranking of EBVs for HD using linear and threshold models were compared. The estimates of genetic parameters and trends were similar for the two models although the ranking of predicted breeding values differed.

In Paper IV, a linear model was used to predict BLUP breeding values, and gave a considerably larger genetic progress compared with phenotypic selection. Thus, although not theoretically optimal, these results indicate that the use of a linear model for genetic evaluation of HD can be expected to substantially enhance selection for improved hip status. Therefore, also considering the importance of a computationally feasible and comprehensible model, it is suggested that a linear model is used for routine prediction of breeding values for HD and ED in Swedish dogs.

Univariate versus Bivariate Models

The genetic correlation between HD and ED was found to be weak and positive (for RW) and not different from zero (for BMD). A low positive genetic correlation between HD and ED was also found in an earlier study of RW in Finland (Mäki *et al.*, 2000). These findings indicate that selection against HD is not expected to reduce the prevalence of ED to any considerable extent, or vice versa. However, because ED includes different entities, with varying prevalence between breeds, the genetic correlation between ED and HD is likely to be breed-dependent. Moreover, ED is not prevalent in as many breeds as HD, implying that several breeds will only be routinely evaluated for HD. Hence, for the sake of consistency across breeds and because of the weak genetic correlations found between HD and ED for RW and BMD, it is suggested that univariate models are used for prediction of breeding values for HD and ED.

Systematic Environmental Effects

As stated earlier, the effect of various systematic environmental factors on evaluation of hip and elbow status implies that the individual's own screening result is an imprecise estimate of its breeding value. Based on the finding that sedation method affected the screening result for HD (Paper I), mandatory recording of the type of chemical restraint used for sedation during hip screening was introduced in Sweden in 2004. This makes it possible to adjust for the effect of sedation method in the model for prediction of breeding values for HD. Hence, based on the results presented in this thesis it is suggested that the fixed effects of sedation method (for HD), sex, age at screening, birth month and year of examination, as well as the random effect of veterinary clinic by year of examination, are included in the model to predict breeding values for HD and ED, respectively. As a result, the trend in EBVs will yield a more accurate reflection of the genetic improvement than the phenotypic trend.

The estimates of variance for the random effect of veterinary clinic by year of examination explained only a small proportion of the phenotypic variance of HD and ED (Paper III). However, by including this effect in the model for prediction of breeding values, it becomes more robust to potential time trends in environmental effects as new data are added. For example, potential changes in routines for hip and elbow screening at some veterinary clinics, which may affect the diagnosis of hip and elbow status, will automatically be adjusted for in the genetic evaluation by the effect of veterinary clinic and year. By having veterinary clinic by year of examination as a random rather than a fixed effect, the evaluation will not be unduly affected by small numbers in a subclass.

The effect of panelist was not found to be significant in the preliminary analyses of data for Paper III. However, as the constitution of the group of panelists contracted by the SKC has changed during the later years, this effect could be worth investigating based on more recent data. The effect of panelist was shown to significantly affect ED (but not on HD) in a Finnish study (Mäki *et al.*, 2000). Moreover, data on weight of the dog at the time of hip screening is being recorded by the SKC since 2005. Limited food consumption and body growth is known to influence the development of HD (e.g., Kealy *et al.*, 1997). Furthermore, two recent studies found significant phenotypic correlations between prevalence of HD and body mass index (Comhaire & Snaps, 2008; Roberts & McGreevy, 2010), and another study found high body weight and high intake of fat to be risk factors for ED in Swedish Labrador Retrievers (Sallander *et al.* 2006). Hence, the effect of weight on HD and ED would be interesting to investigate further and to possibly include in the statistical model for prediction of breeding values. Other systematic environmental effects that could be investigated are the maternal effect and the effects of kennel and litter on HD and ED. However, earlier studies of dog populations in other countries have found these effects to have slight or negligible influence on HD or ED or both (Lingaas & Heim, 1987; Distl *et al.* 1991; Mäki *et al.*, 2000; Janutta *et al.,* 2006b). These findings could be explained by the fact that most puppies are separated from their mother and litter mates already around eight weeks of age, i.e., before the major growth period (Sallander *et al.*, 2001).

Practical Considerations

Implementation of breeding value prediction for HD and ED will require some practical considerations. Routines and policies for prediction and publication of EBVs have to be developed. The routine predictions of breeding values for HD and ED will be administered by the SKC and the EBVs will be published on the SKC web site.

Breeding value prediction for improved hip or elbow status will not be implemented in all breeds where these diseases are prevalent. Before introducing EBVs for HD or ED in a dog breed, the status regarding prevalence of radiographic HD/ED and clinical problems related to HD/ED, as well as the number and proportion of dogs screened, will need to be evaluated. The availability of EBVs may lead to an increased focus on HD/ED in selection. Therefore, BLUP for HD or ED should preferably be introduced in breeds where these diseases are of clinical relevance, to avoid unwarranted increase in selection intensity for joint diseases. Moreover, in some breeds, the number or proportion of screened dogs will be too low for breeding values to be predicted with sufficient accuracy. In numerically small populations, introducing BLUP might be inappropriate due to the increased likelihood of co-selecting related animals (Verrier *et al.* 1993).

In the breeds for which breeding value prediction for HD and/or ED is introduced, strategies for the use of EBVs will need to be included in the breed-specific breeding plan. Paper IV showed that phenotypic restrictions based on the screening record (only allowing A and B dogs in breeding) marginally affected the genetic progress for HD and caused a reduction in the overall genetic progress, compared with when dogs with mild dysplasia (grade C) were allowed in breeding. Thus, to use BLUP efficiently in practice, breeding decisions on HD or ED or both should be based on EBVs, and phenotypic restrictions based on the screening result should be avoided. Therefore, the current requirements in the genetic control programmes for HD/ED, stated in terms of phenotypic screening results (i.e., only dogs with normal hip or elbow status are accepted for breeding), will need to be revised and based on the dogs' EBVs instead.

The EBVs have to be updated routinely as additional data on hip or elbow status for the individual dog or its relatives are recorded in the SKC database. Routines and policies for updates and publication of EBVs need to be elaborated. Preferably, new predictions should be made with short time intervals to assure that the EBVs are as accurate as possible and that EBVs, rather than phenotypes, are used as basis for selection.

Optimisation of Breeding Strategies

Selection for improvement of categorically scored hip status using BLUP was shown to enable a larger genetic progress than phenotypic selection

(Paper IV). These results could most likely also be applied to ED, being measured as a categorical trait with about the same heritability as HD. However, as shown in Paper IV, introduction of BLUP will most likely create a higher inbreeding rate, as a result of using information from relatives to predict individual breeding values, thereby increasing the correlation among EBVs of relatives and the probability of co-selecting related animals (Verrier *et al.*, 1993).

In optimised breeding strategies for improved hip and elbow status, both the genetic change in HD/ED and the rate of inbreeding should be considered. By using OCS, the genetic gain can be maximised with a restriction on the rate if inbreeding (Meuwissen & Sonesson, 1998; Grundy *et al.*, 2000). Paper IV showed that using OCS based on BLUP made it possible to lower the rate and onset of inbreeding to approximately the same level as for phenotypic selection, but with a considerably higher genetic progress for HD. However, in practical dog breeding implementation of OCS schemes in routine is most likely difficult as the selection of breeding animals, and the extent to which these are used, mainly are up to the individual breeders. Therefore, alternative strategies to monitor and control the rate of inbreeding need to be elaborated, preferably focusing on constraining the rate of increase in coancestry because it accounts for information on the future rate of inbreeding (Sørensen *et al.*, 2005). The best approach would be to use OCS software to find theoretically optimal genetic contributions, to be used as a basis for guidance of breed clubs and individual breeders in breeding planning. This could for example lead to recommendations or restrictions on the maximum number of litters for individual parents in some breeds. Inbreeding coefficients for each dog and a tool for calculating the inbreeding coefficients for the offspring resulting from a planned mating are already being published at the SKC web site. Additionally, the additive genetic relationship between each dog and the breed as a whole could preferably be published.

The Overall Breeding Programme

Putting the results presented in this thesis in a broader perspective, it is important to emphasise that breeding of dogs involves more than concerns about hips and elbows. The genetic control programmes administered by the SKC have been developed only for diseases with well defined and validated methods for examination and diagnosis. Many breeds have other, less well defined, heritable conditions that may considerably affect the dogs' health. It is therefore important not to focus too much on only one or a few diseases because they are easy to diagnose and to record. Furthermore, besides health traits, many of the major challenges in dog breeding are related to breeding in small populations in combination with a one-sided focus on morphological traits (McGreevy & Nicholas, 1999).

For a sustainable breeding of healthy dogs, an overall breeding programme has to be developed for each dog breed. The breeding programme should consider all traits of importance; health traits, as well as behavioural and morphological traits, taking genetic variation and population structure into account. By including many traits in the breeding goal, the risk of intense selection for only a few traits is lowered. However, only traits that are considered valuable should be included to avoid reduction of the overall genetic progress. It can nevertheless be worthwhile to record other traits, to be able to monitor the development. A broadly defined overall breeding goal is also likely to result in a lower rate of inbreeding compared with one-sided focus on only one or few traits (Sørensen *et al.* 1999). The introduction of BLUP selection for HD and ED is expected to result in increased selection intensity for these traits. Thus, implementation of BLUP breeding values for other traits in the breeding goal, for example behavioural traits, should be prioritised as well, to avoid too much focus on joint diseases relative to other traits of importance.

The development of breed-specific breeding plans, started by the SKC in 2001, is an important step towards more comprehensive and long-term breeding goals in dog breeding. However, the structure in dog breeding, including many breeders with varying interests and knowledge, often makes it difficult to find agreement on uniform breeding goals. Therefore, continuous information and support to breed clubs and breeders is important for the further development and implementation of these breeding plans into practice.

In many breeds, the breed-specific breeding plans have already been applied for some years. The prerequisites for the breeding programme may change over time not only as a result of selection, but also because of other factors such as "new" diseases emerging, increased knowledge or enhanced tools becoming available. Therefore, evaluation and possibly revision of the goals and strategies is needed routinely. The emergence of a disease that is not previously known in a breed often causes turbulence in the breed club. The first step should be to develop routines for accurate diagnosis and recording. If possible, grading of the disease in more than two categories (healthy versus diseased) is desirable because it enhances the genetic evaluation (Falconer & Mackay, 1996). Moreover, verification that the selection criterion, i.e., the diagnosis of the disease, is closely associated with the breeding goal trait should be done (Paper II). Accurate information about the disease enables analyses of prevalence and mode of inheritance. This kind of information is needed to develop an appropriate breeding strategy. It should be emphasised that intense truncation selection based on phenotypic data, excluding both diseased animals and many of their relatives from breeding, is expected to be an inefficient and uncertain way to manage the situation with a "new" disease emerging (Paper IV). To support breed clubs in the development of appropriate breeding strategies, general breeding recommendations for diseases with different mode of inheritance, as well as for diseases with unknown mode of inheritance, have been elaborated by the SKC[5].

[5] Karin Drotz, the Swedish Kennel Club, personal communication

Conclusions

Radiographic hip status was shown to be strongly associated with subsequent incidence of veterinary care and mortality related to the hip joint, by combining data on hip and elbow health in Swedish dogs from different sources. This indicates that records from hip screening in young adult dogs provide valuable information about later clinical problems related to HD. Moreover, the genetic analyses of screening records for HD and ED showed considerable genetic variation and moderate heritability of both traits. Taken together, these findings suggest that screening records for HD and ED can be used in selection aimed at improved hip and elbow health.

The significant impact of systematic environmental factors, such as sedation method, on radiographic hip and elbow status implies that the individual's screening result alone imprecisely estimates its breeding value and is therefore not the most accurate basis for identification of animals to become parents. This problem can be solved by the use of BLUP, which uses phenotypic records of relatives and simultaneously adjusts for systematic environmental effects. Simulation of selection strategies showed that BLUP selection was superior to phenotypic selection, irrespective of initial HD prevalence, population size and proportion of dogs with a screening record. This suggests that BLUP selection against HD can be expected to be effective in breeds with various population structure and prevalence of HD.

Based on the studies included in this thesis, it is concluded that implementation of BLUP breeding values for radiographic hip and elbow status, instead of phenotypic selection, would enable a more efficient breeding for improved hip and elbow health in Swedish dogs. Because BLUP selection most likely will lead to higher rates of inbreeding, compared with phenotypic selection, the introduction of BLUP in practical breeding should be combined with tools to monitor and restrict the rate of inbreeding.

Future Outlook

Breeding value prediction for HD and ED using BLUP will soon be implemented in Sweden. As concluded in this thesis, the use of BLUP will enable a more effective breeding programme for improved hip and elbow health in Swedish dogs. Considering future breeding of healthy dogs in a broader perspective, the same kind of issues as investigated for HD and ED in this thesis need to be examined also for other heritable diseases in dogs. Firstly, whether the recorded trait is an accurate selection criterion needs to be investigated. To assess this, the genetic variation and heritability of the trait have to be estimated. Moreover, the phenotypic and genetic correlations between the recorded trait and the breeding goal trait should be studied. For an effective and successful breeding of healthier dogs it is important to select for health traits (i.e., disease diagnoses) that are clinically relevant for the dogs' health and well being. Secondly, methods for more accurate genetic evaluation should be implemented also for other diseases to allow for a more effective selection, and to avoid too high selection intensity for joint diseases relative to other important traits. In the next few years, BLUP will probably be introduced for genetic evaluation of other quantitative diseases, as well as for behavioural characteristics in dogs. Because inaccurate genetic evaluation and selection lead to reduced or no genetic progress, these issues are important and call for cooperation between geneticists, veterinarians, breed clubs and kennel clubs.

The Swedish population of most breeds only represent a small part of a larger international population, with considerable exchange of breeding animals between countries. Thus, international cooperation is of uttermost importance for successful breeding programmes. Harmonisation of screening procedures for HD and ED has already advanced considerably in the Nordic countries through the work of the Nordic Kennel Union. However, expanded international collaboration regarding diagnostic procedures, tools for genetic evaluation and breeding strategies is desirable. In the future, joint genetic evaluation, for example in the Nordic countries, for health traits such as HD and ED among genetically connected populations of dogs would enable more accurate genetic evaluation, and facilitate valuable international exchange of genetic material.

The recent advances in molecular genetic technologies and the availability of the canine genome sequence and SNP arrays enhance the possibilities of clarifying the genetic basis of different canine diseases, even for quantitative traits such as HD and ED. Several studies have already identified QTLs on different canine chromosomes that contain genes contributing to HD (Chase *et al.*, 2004; Todhunter *et al.*, 2005; Marschall & Distl, 2007). However, in practical dog breeding molecular genetic tools has so far been implemented only for qualitative traits, by the use of DNA tests for autosomal recessive diseases. The large number of DNA tests for different diseases becoming available is likely to imply increased complexity in the breeding programme of many dog breeds. Hence, prioritisations based on the prevalence and clinical relevance of different diseases will become increasingly important.

Genomic data also for quantitative diseases, such as HD and ED, will possibly be introduced in practical dog breeding in the future. Genomic selection has already been implemented in routine genetic evaluations for dairy cattle (Hayes *et al.*, 2009), and in a recent study by Stock & Distl (2010), the use of genomic selection for HD in dogs was suggested. However, all of these developments are connected with costs that are much higher than those of breeding value prediction using traditional BLUP, at least currently. Because both HD and ED have moderate heritability and are possible to measure in both sexes, quite early in life, the benefit of genomic selection is not likely to be large enough to justify these costs. Implementation of genomic selection would probably be more beneficial for other traits in dogs, such as diseases diagnosed late in life, with low heritability and/or diseases that can only be measured in one sex.

To conclude, the introduction of new tools in practical dog breeding, such as breeding value prediction using BLUP, DNA tests and possibly genomic selection, will require increased support to dog breeders and adaptation of breeding programmes to make use of these tools in the best way. Because dog breeding is of concern not only to individual breeders, but also to kennel clubs, breed clubs, geneticists, veterinarians, authorities and the general public, cooperation between the different parties, at both national and international levels, is important for a successful breeding of healthy dogs.

Avelsarbete för bättre ledhälsa hos svenska hundar

Bakgrund

Höft- och armbågsledsdysplasi (HD och ED) är vanligt i många, framförallt storvuxna, hundraser och orsakar problem och lidande för såväl hundar som hundägare. Försök att genom avelsarbete minska förekomsten av dessa ledsjukdomar har gjorts i Sverige, och i andra länder, under flera decennier. Avelsurvalet baseras på resultat från röntgenundersökning av höft- och armbågsleder, och i de flesta raser används uteslutande hundar med normala (friröntgade) leder i avel. Trots dessa åtgärder har framsteget, i form av en större andel friröntgade individer, i många raser varit otillfredsställande eller stagnerat.

Dagens avelsvärdering som baseras enbart på individens eget röntgenresultat för HD och/eller ED är inte tillräckligt effektiv och ett behov finns av bättre metoder för avelsvärdering av ledhälsa. Både HD och ED är så kallade kvantitativa egenskaper där fenotypen (det vi kan se eller mäta) påverkas av ett flertal gener tillsammans med olika miljöfaktorer. Röntgenbilden ger begränsade möjligheter att beskriva skillnader i ledkvalitet, framförallt för hundar med friröntgade leder. Många hundar hamnar därför i samma klass, till exempel klassade att ha normala höftleder, trots att deras genotyp (genuppsättning) kan skilja sig åt ganska mycket. Detta, i kombination med inverkan av miljöfaktorer, medför att den enskilda hundens röntgenresultat ger en ofullständig bild av dess genetiska förutsättningar.

Förutom bra metoder för avelsvärdering av de egenskaper som avelsurvalet baseras på, är det för ett framgångsrikt avelsarbete av stor vikt att dessa egenskaper är starkt genetiskt korrelerade till de så kallade mål-egenskaperna, det vill säga de egenskaper man vill förbättra. I avelsarbetet för bättre ledhälsa är målet att minska de kliniska problemen relaterade till höft- och armbågsleder genom selektion baserad på röntgenundersökning och gradering av HD och ED vid cirka ett års ålder.

Syftet med denna avhandling var att undersöka möjligheterna till ett effektivare avelsarbete för bättre ledhälsa genom:

- skattning av genetiska och miljömässiga faktorers inflytande på röntgenresultatet för HD och ED (studie I och III)
- utvärdering av sambandet mellan röntgenresultatet för HD och senare kliniska problem samt livslängd (studie II)
- utveckling av en statistisk modell för skattning av avelsvärden för HD och ED, så kallat HD-index och ED-index (studie III)
- jämförelse av avelsstrategier för bättre ledstatus (studie IV)

Sammanfattning av studierna

Data från olika informationskällor kombinerades i analyserna: härstamningsdata och röntgenresultat för HD och ED erhölls från Svenska Kennelklubben (SKK), enkätdata avseende rutiner för höftledsröntgen insamlades från svenska veterinärkliniker och data avseende veterinärvårdsskador och livskador relaterade till HD hämtades från försäkringsbolaget Agria. Dessutom användes simulerade data för jämförelse av avelsstrategier.

Ett starkt samband mellan röntgenresultatet för HD och veterinärvårdsskador samt livskador relaterade till höftlederna påvisades genom att kombinera data från SKK med försäkringsdata (studie II). Detta indikerar att röntgenresultatet ger värdefull information om risken för kliniska problem och förkortad livslängd relaterat till HD. Vidare visade de genetiska analyserna av röntgenresultat för HD och ED på betydande genetisk variation och medelhög arvbarhet för båda egenskaper (studie III). Sammantaget ger dessa resultat stöd för användningen av röntgenresultat för HD och ED i avelsarbetet för bättre ledhälsa.

Faktorer som sederingspreparat, ålder vid röntgen, födelsemånad och kön hade en signifikant effekt på röntgenresultatet för HD och/eller ED (studie I och III). Resultaten bekräftar att avelsvärdering endast baserad på individens eget resultat ger en otillräcklig bild av dess genetiska förutsättningar (nedärvningsförmåga). För en mer korrekt avelsvärdering bör avelsvärden för HD och ED skattas, baserat på röntgenresultatet, med den så kallade BLUP-metoden. Skattning av avelsvärden görs med en statistisk modell som tar hänsyn till och korrigerar för inverkan av olika icke-genetiska faktorer (så kallande systematiska miljöfaktorer). Dessutom inkluderas vid skattningen all tillgänglig information om släktingars resultat. Det skattade avelsvärdet, som brukar kallas för HD-index respektive ED-index, är ett bättre mått på hundens nedärvningsförmåga avseende HD eller ED än enbart individens eget röntgenresultat.

Selektion baserad på HD-index gav ett större avelsframsteg och en snabbare minskning i HD-förekomsten jämfört med selektion enbart baserad på individens eget röntgenresultat för HD, så kallad fenotypselektion (studie IV). Detta kunde visas genom simulering av olika avelsstrategier för bättre ledstatus där det genetiska framsteget, HD-förekomsten och inavelsutvecklingen för fenotypselektion jämfördes med selektion baserad på HD-index. Selektion baserad på HD-index var överlägsen fenotypselektion oberoende av populationsstorlek, HD-förekomst och andel röntgade hundar. Detta indikerar att HD-index kan förväntas vara ett användbart verktyg i raser med olika populationsstruktur och frekvens av HD. De erhållna resultaten kan förväntas vara tillämpbara även för selektion mot ED.

Införande av HD- och ED-index kan förväntas bidra till en ökad inavelsgrad till följd av att också släktingars röntgenresultat inkluderas vid skattningen av avelsvärdet, vilket medför en ökad sannolikhet för att närbesläktade djur selekteras i högre utsträckning. Därför bör introduktion av BLUP-metoden för skattning av HD- och ED-index kombineras med strategier för att övervaka och kontrollera inavelsökningen, framförallt i numerärt små raser.

Slutsatser i korthet

Röntgenresultatet för HD ger värdefull information om risken för kliniska problem och förkortad livslängd relaterat till höftlederna. Detta ger stöd för användningen av röntgenresultat i avelsarbetet för bättre ledhälsa. För en säkrare avelsvärdering bör införande av HD- och ED-index, skattade med den så kallade BLUP-metoden, prioriteras i avelsarbetet för bättre ledhälsa. Vid skattning av HD- och ED-index inkluderas också resultat för släktingar i beräkningarna och hänsyn tas till effekten av olika systematiska miljöfaktorer som påverkar röntgenresultatet, till exempel sederingspreparat. Detta medför möjligheter till ett effektivare avelsarbete för bättre ledhälsa hos våra hundar än vad som hittills varit möjligt med fenotypselektion baserat enbart på den enskilda hundens resultat.

Praktisk tillämpning av resultaten

SKK planerar att i en nära framtid att introducera HD- och ED-index för några raser. De skattade avelsvärdena kommer att publiceras på SKK:s hemsida via tjänsten Avelsdata. I de raser för vilka index för HD och/eller ED införs behövs information om och riktlinjer för hur dessa index bäst ska användas i avelsarbetet. Nuvarande krav på friröntgade höftleder behöver, i raser för vilka index införs, ersättas med krav och/eller rekommendationer relaterade till det skattade avelsvärdet. Dessutom bör strategier för att övervaka och begränsa inavelsökningen utformas parallellt med införandet av index för att undvika en ökning av inavelsgraden.

Till följd av att typ av sederingspreparat vid röntgen visade sig ha en signifikant inverkan på röntgenresultatet för HD, infördes krav på att sederingspreparat ska anges på blanketten för höftledsröntgen för varje hund. Det innebär att information om sederingspreparat finns registrerat i SKK:s databas sedan år 2004 och därmed kan tas med i modellen för skattning av avelsvärden.

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