

Estimation of heritabilities, genetic correlations, and breeding values of four traits that collectively define hip dysplasia in dogs

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Objective—To estimate heritabilities and genetic correlations among 4 traits of hip joints (distraction index [DI], dorsolateral subluxation [DLS] score, Norberg angle [NA], and extended-hip joint radiograph [EHR] score) and to derive the breeding values for these traits in dogs.

Animals—2,716 dogs of 17 breeds (1,551 dogs in which at least 1 hip joint trait was measured).

Procedures—The NA was measured, and an EHR score was assigned. Hip joint radiographs were obtained from some dogs to allow calculation of the DI and DLS score. Heritabilities, genetic correlations, and breeding values among the DI, DLS score, NA, and EHR score were calculated by use of a set of multiple-trait, derivative-free, restricted maximum likelihood computer programs.

Results—Among 2,716 dogs, 1,411 (52%) had an estimated inbreeding coefficient of 0%; the remaining dogs had a mean inbreeding coefficient of 6.21%. Estimated heritabilities were 0.61, 0.54, 0.73, and 0.76 for the DI, DLS score, NA, and EHR score, respectively. The EHR score was highly genetically correlated with the NA ($r = -0.89$) and was moderately genetically correlated with the DI ($r = 0.69$) and DLS score ($r = -0.70$). The NA was moderately genetically correlated with the DI ($r = -0.69$) and DLS score ($r = 0.58$). Genetic correlation between the DI and DLS score was high ($r = -0.91$).

Conclusions and Clinical Relevance—Establishment of a selection index that makes use of breeding values jointly estimated from the DI, DLS score, NA, and EHR score should enhance breeding programs to reduce the incidence of hip dysplasia in dogs. (*Am J Vet Res* 2009;70:483–492)

Hip dysplasia in dogs is a polygenic disease characterized by hip instability that results in secondary osteoarthritis, lameness, and physical disability.¹ Medical and surgical management of the condition have economic and emotional impacts on dog owners and breeders. As a complex trait, HD is caused by genetic and environmental factors that influence expression of the primary trait and the severity of secondary osteoarthritis.² Factors that affect expression of HD and development of secondary osteoarthritis in dogs include sex, age, and body weight.^{2–6} Many genes likely underlie expression of HD, most of which have a small additive effect (polygenes), but some of which likely have larger effects.^{4,7,8}

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ABBREVIATIONS

BLUP	Best linear unbiased prediction
HD	Hip dysplasia
DI	Distraction index
DLS	Dorsolateral subluxation
EHR	Extended-hip joint radiograph
NA	Norberg angle
OFA	Orthopedic Foundation for Animals
PennHIP	University of Pennsylvania Hip Improvement Program

In North America, selection methods to improve the genetic composition of dog breeds and, in so doing, improve hip joint conformation have been based on radiographic hip joint screening, semiopen (OFA) and closed (PennHIP) hip joint registries, and organized breeding programs.^{9–11} Through these breeding strategies, HD was determined to be heritable, and selective breeding efforts reduced the prevalence of HD.¹² For example, the prevalence of HD in German Shepherd Dogs at 12 to 16 months of age decreased from 55% to 24% after 5 generations of selection,¹² and the prevalence of HD in Labrador Retrievers decreased from 30% to 10%.^{13,14} Selective breeding is less effective when a single phe-

notype is used as the selection criterion^{15–22} than when estimated breeding values are used.^{23,24}

Because HD has been so difficult to accurately define and eliminate in dogs, much effort has been directed at developing and comparing the accuracy of radiographic screening tests.^{3,25} The most widely used method for diagnosis in North America is the ventrodorsal EHR, commonly referred to as the OFA method.²⁶ From this radiographic image, a subjective EHR score is obtained. Objective measurements include the DI,²⁷ DLS score,^{3,28,29} and NA.³⁰ Heritabilities of these traits reportedly range from 0.10 to 0.68.³¹

Because the objective hip joint traits and the EHR score are modestly correlated with each other at the phenotypic level,^{25,29,32,33} the estimates of heritabilities and breeding values derived from a multiple-trait model, which incorporates genetic and environmental correlations among the traits, would be more accurate than if they were derived from a single trait.^{34,35} More importantly, the genetic correlations estimated from a multiple-trait model would provide the essential values by which a selection index could be derived to integrate the breeding values of all the traits.³⁶ Selective breeding based on these combined breeding values should be more effective in reducing the prevalence of such a complicated trait than breeding decisions made on the basis of a breeding value for a single trait.³⁷

Although heritabilities of radiographic hip joint measurements have been investigated in various dog breeds in various environments,^{33,38–41} estimates of genetic correlations among values used to judge hip joint quality are limited. The purpose of the study reported here was to estimate genetic correlations among the DI, DLS score, NA, and EHR score and their heritabilities in a multiple-trait model for subsequent use in deriving a breeding value for each of these 4 traits of hip joints.

Materials and Methods

Animals—Dogs used in the study originated from closed breeding colonies at the Baker Institute for Animal Health at Cornell University, the Guiding Eyes for the Blind in Yorktown Heights, NY, or those admitted to the Cornell University Hospital for Animals for radiographic evaluation from January 1999 through October 2007. Multiple radiographic evaluations were available for some dogs. The hip joints of the Baker Institute dogs were commonly radiographed at 8 to 12 months of age. The hip joints of the dogs at the Guiding Eyes for the Blind were routinely radiographed at 14 to 18 months of age. Dogs admitted to the Cornell University Hospital for Animals were radiographed at any age > 8 months.

Hip dysplasia scoring—As is typical in North America, an EHR was used to assess conformation of each hip joint by assigning a subjective rating of excellent, good, or fair to the joint and borderline and mild, moderate, or severe to the degree of hip dysplasia evident (EHR score). The NA³⁰ was measured from the EHR and ranged from 50° (a subluxated hip joint) to 123° (a hip joint phenotypically unaffected by HD). The maximum amount of lateral femoral head distraction from the acetabulum (ie, the DI) was measured through the PennHIP by means of a radiograph obtained with

the hip joint in the distraction position. Labrador Retrievers with a DI < 0.3 to 0.4 at 8 months of age were presumed to have a > 80% probability of not developing secondary osteoarthritis in hip joints and were classified as unaffected by HD. Those with a DI > 0.7 were presumed to have a high probability of developing osteoarthritis in hip joints and were classified as affected with HD.^{42–46} The PennHIP also involves assessment of EHRs to determine hip joint conformation and whether secondary osteoarthritis exists. When no indication of trauma was evident on the EHR, detection of secondary osteoarthritis in hip joints was believed to be indicative of antecedent HD. The DLS score was measured as the percentage of femoral head covered by the dorsal acetabulum with the hip joint in a natural, weight-bearing position.^{3,25,29,47}

Higher breeding values for the NA and DLS score indicated a better hip joint (ie, less dysplastic), whereas lower breeding values for the DI and EHR score indicated the same thing. Body weight, breed, and sex were recorded when the hip joints were radiographed. Breeds represented by < 10 dogs were removed from subsequent statistical analyses.

Pedigree—Ancestors of each dog were traced back until no parent could be identified. Dogs for which hip joint traits had not been measured were used to genetically connect the dogs from which measurements had been obtained. The additive relationship (kinship) matrix (2,716 × 2,716) was calculated from the pedigree by means of the tabulate method.^{48,49} The calculation began with dogs at the highest (earliest) generation and carried all the way to the dogs without progeny. The diagonals of the matrix were equal to 1 plus the inbreeding coefficient.⁵⁰ The inbreeding coefficient was set at 0% for dogs with unknown parents or no common ancestor within the depth of pedigree tracked for their parents. The kinship coefficient (ie, coancestry) between each pair of dogs was also calculated and was equivalent to the inbreeding coefficient of the hypothetical progeny of each pair (ie, the probability that 2 alleles, sampled at random from each dog, were identical by descent).

Statistical analysis—Summary data regarding signalment of dogs are presented as mean ± SD. A multiple-trait model was used to fully explore relationships among dogs and among hip joint traits. The most dysplastic hip joint of each dog (highest EHR score and DI and lowest DLS score and NA of the 2 hip joints for each dog) was used as the measurement. To improve the accuracy for the prediction of breeding values for each dog and its relatives, multiple measurements from different ages were used whenever available. In addition to providing estimates of genetic correlation among hip joint traits, the multiple-trait model provided accurate predictions of breeding values. In matrix notation, the multiple-trait model was as follows:

$$y = X\beta + Zu + e,$$

in which y is the vector of phenotypic values for the 4 traits (DI, DLS score, NA, and EHR score), β is the vector of fixed effects for sex and breed (categorical vari-

ables) and age and body weight (continuous variables), u is the vector of unknown random additive genetic effects (the estimate of u is referred to as the BLUP or the breeding value), and e is the vector of residual terms. The X and Z are known incidence matrices.

For the random effects, it was assumed that u was normally distributed with a mean of 0 and a variance of G , where $G = G_0 \otimes A$. It was also assumed that e was normally distributed with a mean of 0 and a variance of R , where $R = R_0 \otimes I$. The variables G_0 and R_0 are unknown 4×4 genetic and residual covariance matrices, respectively, for the 4 hip joint traits; A is the additive relationship matrix; and I is the identity matrix. Operator \otimes is the direct product of 2 matrices, which is also referred to as the Kronecker or Zehfuss product. Consequently, the covariance of y (V) is calculated as $V = ZGZ^T + R$, where operator T is transposed. The estimate of β and prediction of u are $\beta = (X^T V^{-1} X)^{-1} X^T V^{-1} y$ and $u = (GZ^T V^{-1}) X (y - X\beta)$, where the operator -1 is inverse and the symbol $-$ represents general inverse.

Restricted maximum likelihood estimates were obtained for unknown variables G_0 and R_0 by use of a set of multiple-trait, derivative-free, restricted maximum likelihood software packages that contained 3 programs.^{51,a} Through use of the first program, the additive relationship matrix was calculated directly from the pedigree; then its inverse matrix and the determinant of the original matrix were evaluated to estimate the log-likelihood function. The inbreeding coefficient, defined as the probability that 2 alleles at any locus are identical by descent,⁵² was calculated for each dog. The inbreeding coefficient was calculated by means of a tabular method described elsewhere.^{48,49} The second program was used to prepare coefficients for the mixed model equation on the basis of a statistical model with fixed and random factors for single- or multiple-trait analysis. The third program was used to solve the mixed-factor linear

equation and calculated the estimates of the variance components that maximized the restricted likelihood given the phenotypic data.⁵⁴

A single trait-by-trait analysis was conducted first. The estimates of additive genetic variance and residual variance were used as the starting values for the 2-trait analysis on all pairwise combinations of the DI, DLS score, NA, and EHR score. Variances from the single-trait analyses and covariances estimated from 2-trait analyses were used as the starting values for the 4-trait analysis. Heritability was defined as the ratio of the additive genetic variance to the total variance (the sum of additive genetic variance and residual variance). In the final multiple-trait analysis, iterations were assumed to have converged when the variance of -2 times the log-likelihood used in the simplex search algorithm was $< 10^{-9}$. To ensure a global maximization in the log-likelihood, a restart of the computer programs was performed, with the converged values used as the restarting points. Restarts were performed until the difference of the $-2(\log\text{-likelihood})$ from 2 consecutive runs was < 0.01 . Estimates reported in the results section are all from the 4-trait analysis. Breeding value accuracy was estimated as the square root of $(1 - PEV/\sigma_a^2)$, where PEV is the error variance of predicted breeding values and σ_a^2 is the additive genetic variance.

Results

Animals—The final data set contained 1,551 dogs with at least 1 of the 4 radiographic hip joint measurements. Seventeen breeds were represented, including Labrador Retriever, Greyhound, their crossbreed offspring, and 14 others. Mean \pm SD age of dogs was 22.98 ± 22.11 months (range, 3 to 136 months). Mean body weight of dogs was 29.30 ± 6.43 kg

Table 1—Pedigree structure and inbreeding coefficient values within breed for dogs with a history of HD from closed breeding colonies and a veterinary teaching hospital.

Breed	G	Nt	Nb	Np	Nu	Ni	Mean	SD	Min	Max
(F ₁ × L) × (F ₁ × L)	5	31	31	0	0	31	0.06	0.03	0.01	0.08
American English Coonhound	1	22	0	0	22	NA	NA	NA	NA	NA
Australian Shepherd	6	42	39	0	3	4	0.10	0.06	0.06	0.19
Border Collie	1	50	8	0	42	NA	NA	NA	NA	NA
Border Terrier	5	20	20	0	0	NA	NA	NA	NA	NA
Bullmastiff	1	10	2	0	8	NA	NA	NA	NA	NA
F ₁ × Greyhound	5	33	33	0	0	NA	NA	NA	NA	NA
F ₁ × L	5	87	87	0	0	87	0.05	0.04	0.01	0.13
German Shepherd Dog	4	174	138	4	32	60	0.14	0.09	0.01	0.33
Golden Retriever	9	224	191	4	29	65	0.08	0.06	0.01	0.25
Great Dane	13	56	30	1	25	3	0.10	0.13	0.03	0.25
Greyhound	6	16	0	0	16	NA	NA	NA	NA	NA
Hound crossbreed	1	11	0	0	11	NA	NA	NA	NA	NA
L	17	1,771	1,559	22	190	1,048	0.06	0.04	0.01	0.32
F ₁	5	42	10	16	16	NA	NA	NA	NA	NA
Newfoundland	8	62	45	0	17	NA	NA	NA	NA	NA
Rottweiler	9	65	47	0	18	7	0.03	0.02	0.01	0.07

G = Generation depth. Nt = Total number of dogs. Nb = Number of dogs for which both parents were known. Np = Number of dogs for which only 1 parent was known. Nu = Number of dogs for which neither parent was known. Ni = Number of inbred dogs. Min = Minimum inbreeding value. Max = Maximum inbreeding value. F₁ = First filial generation resulting from a cross between a Labrador Retriever and a Greyhound. L = Labrador Retriever. NA = Not available.

Table 2—Number of measurements used in the calculation of various scores for degree of HD in dogs from closed breeding colonies and a veterinary teaching hospital that were radiographically evaluated for hip dysplasia.

Breed	DI	DLS score	NA	EHR score
(F ₁ × L) X (F ₁ × L)	23 (23)	23 (23)	22 (22)	21 (21)
American English Coonhound	0	21 (21)	22 (22)	22 (22)
Australian Shepherd	0	0	15 (15)	13 (13)
Border Collie	0	39 (39)	74 (72)	67 (48)
Border Terrier	0	0	11 (10)	10 (8)
Bullmastiff	0	0	12 (12)	11 (10)
F ₁ × Greyhound	33 (33)	33 (33)	33 (33)	33 (33)
F ₁ × Labrador Retriever	79 (79)	88 (88)	88 (88)	88 (87)
Greyhound	16 (16)	16 (16)	16 (16)	16 (16)
German Shepherd Dog	13 (13)	20 (20)	98 (96)	92 (84)
Golden Retriever	0	0	43 (43)	49 (47)
Great Dane	0	0	37 (37)	40 (36)
Hound crossbreed	0	0	10 (10)	11 (11)
L	337 (322)	114 (114)	1,049 (1,008)	832 (747)
F ₁	42 (42)	20 (20)	42 (42)	41 (41)
Newfoundland	10 (10)	0	38 (37)	34 (31)
Rottweiler	0	0	25 (25)	23 (20)
Total	553 (538)	374 (374)	1,635 (1,588)	1,403 (1,275)

Values in parentheses are the number of dogs evaluated in each category. Some dogs had > 1 measurement/type of score.
See Table 1 for remainder of key.

(range, 5.7 to 57.7 kg). Males (46%) and females (54%) were approximately equally represented.

Hip dysplasia scores—Most of the dogs were Labrador Retrievers or their offspring from crossbreeding with Greyhounds (F₁, F₁ backcrosses to Labrador Retrievers or Greyhounds, and F₂ offspring; Table 1). Some traits were measured at multiple ages. The mean number of measurements per dog was 1.3, 1.0, 1.2, and 1.1 for the DI, DLS score, NA, and EHR score, respectively. The DLS score ranged from 85% for tight-hipped Greyhounds to as low as 19% for the most dysplastic dogs. The NA and EHR score were recorded for most dogs, but the DI and DLS score were only available in records from the Baker Institute for Animal Health at Cornell University. Because the NA and EHR score were measured on more dogs than were the DI and DLS score, higher accuracy was expected for the NA and EHR score. Representation of each variable among the various breeds was summarized (Table 2). Values for NA, DLS score, DI, and EHR score were also summarized (Table 3). All 4 hip joint radiographic traits were measured only for Labrador Retrievers, Greyhounds, and their crossbreed offspring and German Shepherd Dogs. For other breeds, only 1 to 3 traits were measured.

Pedigree—A total of 1,165 ancestors was added to the pedigree, which contained 2,716 dogs, including 1,498 dogs from the Guiding Eyes for the Blind organization, 571 from the Baker Institute for Animal Health, 425 from the Cornell University Hospital for Animals, and 222 ancestors traced from the database (Table 1). The role of the 1,165 dogs without a measurement of hip joint quality was to genetically connect the 1,551 dogs with measurements. The most complex generation involved a family of Labrador Retrievers from the Guiding Eyes for the Blind, which included 1,236 connected dogs over 17 generations from a particular male dog.

Table 3—Values of the DI, DLS score, NA, and EHR score in dogs from closed breeding colonies and a veterinary teaching hospital that were radiographically evaluated for HD.

Trait	No. of records	Mean	SD	CV	Min	Max
DI	553	0.55	0.19	0.34	0.07	1
DLS score (%)	374	53.68	13.31	0.25	19.6	80.0
NA (%)	1,635	105.05	7.42	0.07	56	120
EHR score	1,403	2.28	1.52	0.66	1	7

CV = Coefficient of variation.
See Table 1 for remainder of key.

Among 2,716 dogs, about half (859 progeny and 552 founders; 53%) had an inbreeding coefficient of 0%. The remainder had a mean inbreeding coefficient of 6.21%. The highest inbreeding coefficients (31.3% and 37.7%) were obtained for only a few dogs. Inbreeding coefficients and pairwise kinship coefficients were summarized (Figures 1 and 2). Because mating did not occur for any breeds other than Labrador Retriever and Greyhound, > 80% of the total pairs of dogs had unknown coancestries of 0.

Hip joint traits—The estimated effects of age, sex, body weight, and breed on the 4 hip joint traits were summarized (Table 4). Breed of dog had the largest influence on the hip joint trait statistics. The influence of dog age, body weight, and sex on the hip joint traits was minimal. The mean NA for Labrador Retrievers was not significantly different from that of Australian Shepherds, Border Collies, Border Terriers, Bullmastiffs, or Rottweilers. Whereas American English Coonhounds, German Shepherd Dogs, Golden Retrievers, Great Danes, Newfoundlands, and Bullmastiffs had smaller NAs (ie, lower-quality hip joints) than Labrador Retrievers ($P < 0.01$ for all), Greyhounds had larger ($P < 0.01$) NAs (ie, higher-

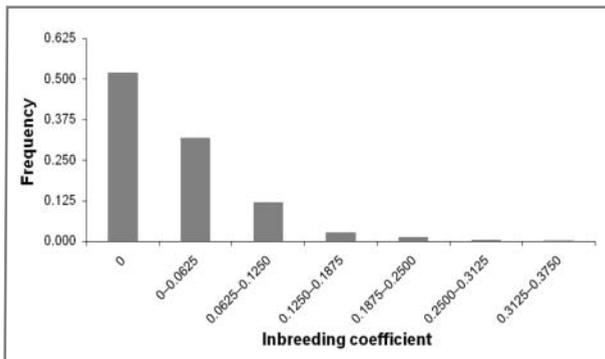


Figure 1—Distribution of inbreeding coefficients among 2,716 dogs from 2 closed breeding colonies and dogs admitted to a veterinary teaching hospital.

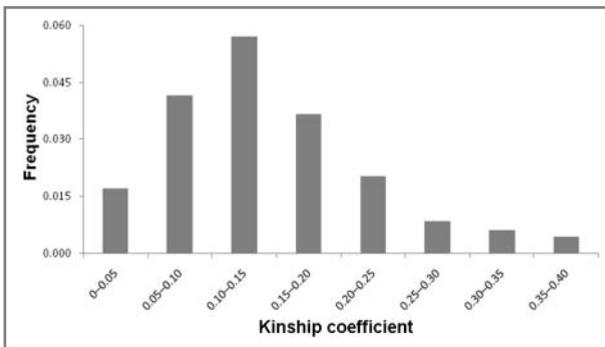


Figure 2—Distribution of pairwise kinship coefficients among 2,716 dogs from 2 closed breeding colonies and dogs admitted to a veterinary teaching hospital. The nonzero pairwise kinship coefficient frequencies in the graph sum to 19.6%. The rest (80.4%) were zeros and removed from the graph.

quality hip joints). A similar pattern was evident for EHR scores.

The 4 hip joint traits had medium to high heritability (Table 5). The EHR score had a high genetic correlation with the NA (−0.89), and the genetic correlation between the DI and DLS score was also high (−0.91). The medium to high heritability for the 4 traits was also evident in the pattern of breeding values during the years when dogs were born (Figure 3). Selective breeding appeared effective at improving mean scores for the 4 hip joint traits over time, particularly since the mid-1990s.

The accuracy of a breeding value for a dog was influenced by whether measurements were made on that dog, whether the parents were measured, and the number of measured progeny (Table 6). The more progeny of a breeding pair that were measured, the higher the accuracy of the breeding value.

The results of selective breeding were also evident in the relationship between breeding values and their accuracy (Figure 4). Over half of the Labrador Retrievers were bred at the Guiding Eyes for the Blind facility. Dogs with more accurate breeding values produced more progeny, with a clustering of breeding values with higher accuracy indicative of better hip joint conformation. In other words, such dogs had larger NAs and DLS scores (positive breeding values) and smaller DIs and EHR scores (negative breeding values), which indicated that the selective breeding practices of the Guiding Eyes for the Blind program which are based on the NA and EHR score, were effective in improving hip joint conformation in dogs. Because the DI and DLS score are genetically correlated to the NA and EHR score, an indirect selection response on the DI and DLS score was

Table 4—Estimates of the fixed effects of age, body weight, sex, and breed on 4 traits of hip joints in 1,551 dogs.

Factor	DI		DLS score		NA		EHR score	
	Estimate	SE	Estimate	SE	Estimate	SE	Estimate	SE
Age	−0.0024	0.0006	0.0145	0.0523	0.0059	0.0057	0.0055	0.0006
Body weight	−0.0019	0.0014	−0.2295	0.1211	−0.0725	0.0233	0.0019	0.0027
Sex								
Male	0.0000	—	0.0000	—	0.0000	—	0.0000	—
Female	0.0101	0.0125	0.1393	1.1077	0.0185	0.2284	−0.1183	0.0278
Breed	−0.1858	0.0188	11.9774	1.4521	7.2317	0.6276	−1.6996	0.1027
American English Coonhound	NC	NC	3.0961	4.2321	−8.3623	0.7942	0.6472	0.1302
Australian Shepherd	NC	NC	NC	NC	0.3094	0.8607	−1.0601	0.1464
Border Collie	NC	NC	8.7490	4.1765	−0.9133	0.5503	−0.4749	0.0935
Border Terrier	NC	NC	NC	NC	2.0217	1.0315	−1.0651	0.1732
Bullmastiff	NC	NC	NC	NC	−1.5697	0.9290	0.3121	0.1545
F ₁ × Greyhound	−0.2323	0.0158	12.4225	1.2815	5.6298	0.5170	−0.9745	0.0832
F ₁ × L	−0.0404	0.0113	2.1218	0.9417	2.9204	0.3275	−0.5181	0.0543
Greyhound	−0.3197	0.0220	22.3641	1.6509	4.5360	0.7278	−0.8040	0.1158
German Shepherd Dog	−0.0519	0.0250	5.6813	1.6203	−2.9855	0.3315	0.6037	0.0519
Golden Retriever	NC	NC	NC	NC	−3.4451	0.4753	0.3695	0.0721
Great Dane	NC	NC	NC	NC	−2.5642	0.5167	0.4075	0.0802
Hound crossbreed	NC	NC	NC	NC	−3.7070	1.0207	1.0194	0.1587
L	0.0000	—	0.0000	—	0.0000	—	0.0000	—
F ₁	−0.1162	0.0142	15.8625	1.5228	3.2860	0.4561	−0.9796	0.0740
Newfoundland	0.2360	0.0698	NC	NC	−4.8545	0.6348	1.2401	0.1062
Rottweiler	NC	NC	NC	NC	0.6941	0.7189	0.4829	0.1185

NC = Not calculated. — = Not applicable.
See Table 1 for remainder of key.

Table 5—Heritabilities (diagonals from top left to bottom right), genetic correlations (values below diagonals), and residual correlations (values above diagonals) among the DI, DLS score, NA, and EHR score in 1,551 dogs from breeding colonies and a veterinary teaching hospital that were evaluated for HD.

Trait	DI	DLS score	NA	EHR score
DI	0.61	-0.16	0.00	-0.02
DLS score	-0.91	0.54	0.34	-0.18
NA	-0.69	0.58	0.73	-0.22
EHR score	0.69	-0.70	-0.89	0.76

also detected. The EHR score and NA were predicted with highest accuracy, indicating more intensive selection was applied for these 2 traits.

Discussion

The opportunity for reduction of the incidence of HD in dogs by selective breeding on the basis of results of hip joint radiographs has been available for over half a century. In 1966, the OFA established a registry of inherited orthopedic traits in dogs.⁵⁵ Its initial mission

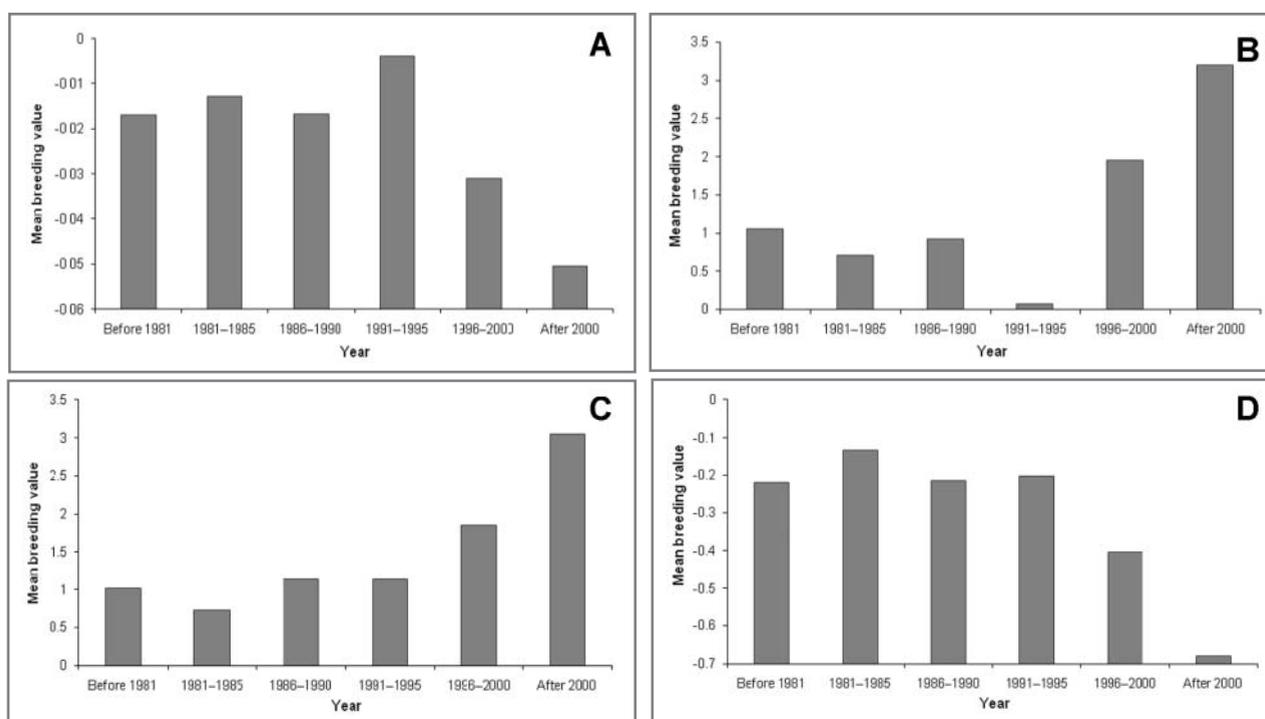


Figure 3—Mean breeding values for DI (A), DLS score (B), NA (C), and EHR score (D) estimated by means of the BLUP method for 2,716 dogs (1,551 phenotyped dogs and 1,165 ancestors) from 2 closed breeding colonies and veterinary teaching hospital born from 1966 through 2006. Lower or negative breeding values for the DI and EHR score reflect good hip joint conformation, whereas higher (positive) breeding values for the DLS score and NA reflect the same thing.

Table 6—Relationship between accuracy of breeding value and percentage of dogs that were measured on themselves, percentage of sires measured, percentage of dams measured, and mean number of progeny measured per sire and per dam in dogs evaluated for hip joint quality.

Trait	Accuracy	No. of dogs	Percentage of dogs measured			Mean No. of progeny	
			Self	Sire	Dam	Per sire	Per dam
DI	> 0.90	58	100.00	96.55	91.38	4.34	4.58
	0.85–0.90	195	100.00	92.82	92.31	0.97	0.97
	0.60–0.85	1,138	14.76	13.80	12.74	0.18	0.19
	< 0.60	1,325	0.00	2.04	0.68	0.78	2.33
DLS score	> 0.90	3	100.00	33.33	100.00	78.00	26.00
	0.85–0.90	109	73.39	50.46	77.98	3.53	2.28
	0.60–0.85	1,218	23.81	12.23	16.42	0.55	0.41
	< 0.60	1,386	0.00	0.36	0.14	0.80	2.00
NA	> 0.90	400	98.75	63.75	63.75	3.37	3.37
	0.85–0.90	863	98.49	50.17	48.32	0.33	0.35
	0.60–0.85	622	13.99	47.11	42.12	0.93	1.04
	< 0.60	831	0.00	1.68	1.08	7.14	11.11
EHR score	> 0.90	574	97.21	65.16	65.16	1.99	1.99
	0.85–0.90	664	91.27	34.04	41.11	0.75	0.62
	0.60–0.85	657	8.22	45.97	46.27	0.90	0.89
	< 0.60	821	0.00	1.58	1.58	7.00	7.00

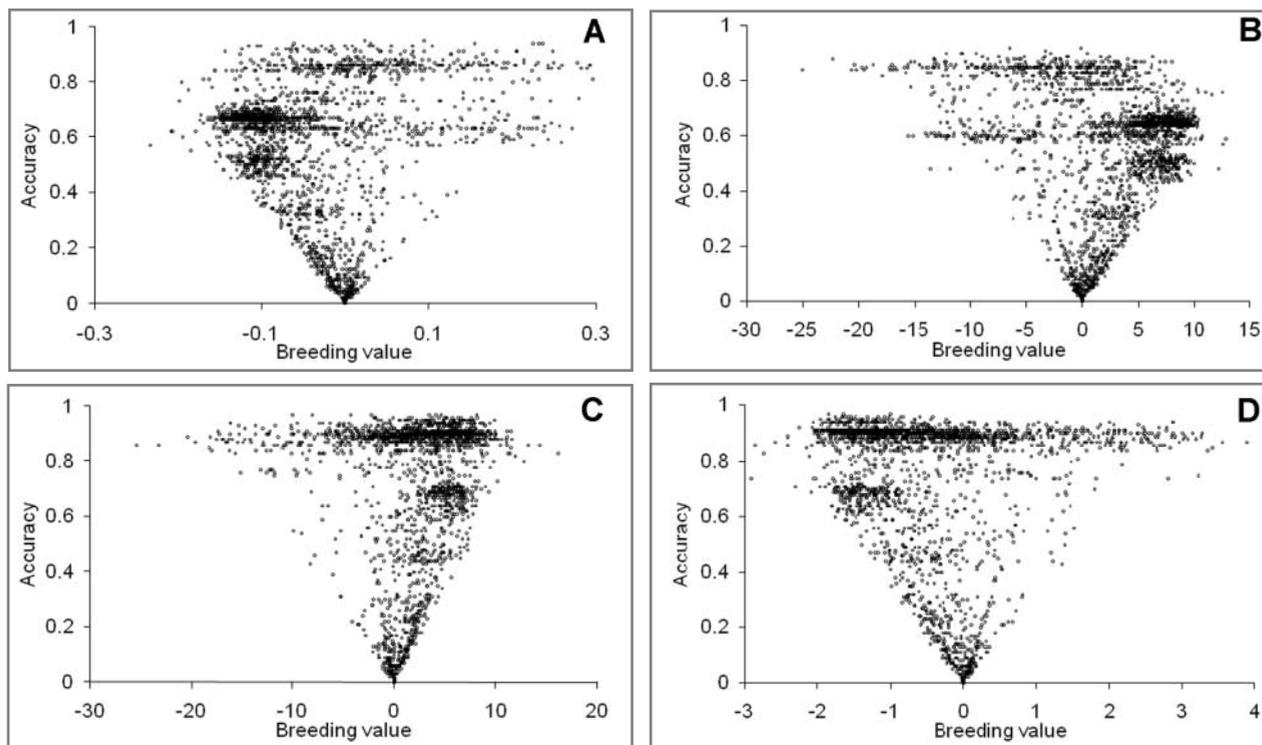


Figure 4—Distribution of breeding values of 2,716 dogs from 2 closed breeding colonies and a veterinary teaching hospital compared with the accuracy of those values for the DI (A), DLS score (B), NA (C), and EHR score (D). Lower or negative breeding values on the DI and EHR score reflect better hip joint conformation as do higher (positive) breeding values for the DLS score and NA. Clustering of values at the top of the accuracy range (0.75 to 1.0) and clustering of values at the top of the accuracy range (0.75 to 1.0) and the right side of breeding values for DLS scores and NAs or the left side for DIs and EHR scores is evidence of effective selection to reduce HD.

was to provide radiographic evaluation, data management, and genetic counseling for reduction of the incidence of HD. Since then, improvement in hip joint phenotypes in North American purebred dogs has been modest.^{15–19,22} This is partly attributable to the preferential submission of radiographs to the OFA for hip joint certification, the preference of owners regarding publication of their dogs' EHR scores on the OFA Web site, and the difficulty breeders and dog owners have in making use of all the pedigree and phenotype information available in the OFA registry. Such semiopen databases could be used to provide quality scores for hip joints and breeding values of dogs that are based on genetic correlations among several traits of hip joints. However, one cannot ignore the fact that selective breeding on the basis of hip joint phenotype alone would be more effective if it were used by all breeders and purchasers of purebred dogs. Lack of compliance by breeders and owners with including hip joint phenotypes (ie, information on hip joint traits) for some radiographed dogs or not making such information available has led to bias in the databases.²²

The breeding value in its earliest use was also called the selection index.^{56–58} The selection index was based on integration of genetic and phenotypic information from each animal and its relatives and yielded better results than phenotypic selection alone for desired traits. As was evident in the present study (Table 6), the accuracy of the selection index of a subject increases when the phenotype information from its close relatives (eg, progeny and ancestors) is included in the

estimation. With the assumption that environmental effects were perfectly estimated, which was not valid in most situations, the selection index was developed into the BLUP.⁵⁹ The BLUP breeding strategy has been used successfully for genetic improvement, particularly in livestock, and has also been applied in closed colonies of dogs.^{13,14}

Implementation of the BLUP strategy was enhanced by methods of variance component estimation, such as restricted maximum likelihood.⁶⁰ Variance components attributable to additive genetic and residual effects have been estimated and the heritability of HD has been derived in Finnish Rottweilers.⁴⁰ Results of the present study indicated that the establishment of a selection index that included the DI and DLS score along with the NA and EHR score could be more effective in reducing the incidence of HD than use of a single phenotypic measurement. An EHR score and NA were measured in most dogs, whereas the DI and DLS score were obtained less commonly. Even so, we were able to infer the DI and DLS score on the basis of the pedigree relationships and genetic correlations among the hip joint traits. On the other hand, most dogs with a DI and DLS score also had an NA and EHR score, and this provided the essential information to estimate the genetic correlations among them.

The heritability of each hip joint trait estimated in the present study was moderate to high for a complex trait and may have been overestimated because of the restricted population evaluated (many of the dogs were reared in controlled environmental conditions).

Generally, most breeders and dog purchasers will only have access to either an EHR score from the OFA or a DI when they collaborate with a veterinarian who is a member of the PennHIP. Although variable environmental conditions can affect genetic improvement, selection accuracy for genetic potential of hip joints with good quality has been low in the general population of dogs because most selective breeding is performed on the basis of phenotype alone.

A preferable selection option for breeders and purchasers of dogs would be selective breeding based on genetic values of hip joint conformation or selection indices. The mean breeding values in our sample of dogs during the study period clearly suggested the genetic improvement that can be gained through selective breeding. In our study, the breeding value and its accuracy for each dog were calculated for the DI, DLS score, NA, and EHR score measured on the most dysplastic hip joint of 1,551 dogs. We identified a cluster of dogs with highly accurate breeding values that also indicated good hip joint conformation. The Labrador Retrievers from the Guiding Eyes for the Blind program constituted of over half of the dogs in the study. Selection of dogs for hip joint quality resulted in genetic improvement predominantly in the last 10 to 15 years, when strong genetic selection pressure was applied on dogs at the Guiding Eyes for the Blind on the basis of phenotypes in the mid-1990s, and the BLUP method was implemented to apply additional pressure on hip joint conformation in 2004. Pedigrees with more ancestors and relatives also became available over the last 10 years, compared with the amount of data available in the previous decade.

We propose selection indices derived from hip joint traits of dogs in the public OFA database be applied when selecting of breeding dogs and puppies for purchase. This approach should improve hip joint conformation of dogs in subsequent generations. Although selective breeding based on choice of sires would be more efficient than that based on choice of dams, selective breeding based on choice of both sexes would be preferable. Breeding values and inbreeding coefficients for the most recent generations of dogs in the OFA database could be estimated and provided to the public upon request so that dogs with optimal hip joint conformation could be selected as breeding dogs and for purchase.

Results of the multiple-trait modeling in the present study strongly suggested that a single hip joint radiograph does not provide as much information about a dog's genetic potential as a combination of measurements of hip joint conformation. Thus, a single hip joint measurement is insufficient to provide a basis for breeding decisions. In the PennHip, a distraction projection is used to calculate the DI, and the EHR score is used to assess whether HD and secondary osteoarthritis exist. However, that database is not open. In another study,³³ we found that a combined NA and DLS score or DI provided a more accurate prediction of secondary osteoarthritis in hip joints than a single trait predictor in young adult Labrador Retrievers, Greyhounds, and their crossbreed offspring.³³ If the DI and EHR scores accumulated for each dog in the PennHIP were com-

bined into a selection index and made available in a user-friendly interface for dog owners and breeders, additional improvement in hip joint conformation would likely ensue. As a start, such information could be provided to dog owners as part of the information they receive when their dog's hip joints are evaluated.

As genetic markers become available for quantitative trait locus detection, genetic selection based on results of BLUP estimated from phenotypes could be developed into marker-assisted selection based on results of BLUP estimated from marker genotypes. Marker-assisted selection is superior to genetic selection by means of BLUP based on phenotypes alone.^{61,62} The BLUP based on genetic markers of susceptibility and resistance to HD will be identified in the future, and when identified, this information could be combined with phenotype breeding values to improve selective breeding programs. The high genetic correlation between the EHR score and NA and between the DLS score and DI in our study suggested that common genes may be associated with these 2 pairs of hip joint traits. In support of this supposition is the preliminary finding from a molecular genetics study⁷ that some quantitative trait loci identified as contributing to HD for a single hip joint trait have pleiotropic effects on other hip joint traits or that single traits are associated with linked loci. This suggests that identifying genes that underlie the NA and EHR score and the DI and DLS score will lead to the most complete understanding of the molecular genetic basis of HD. The addition of genetic marker breeding values for the DI or DLS score to a hip joint selection index should additionally improve hip joint quality because some of the underlying mutations that contribute to these 2 traits are likely different from those underlying the NA and EHR score.

In the present study, proportions of records that were missing for each of the 4 hip joint traits varied. Only 11% of the 1,551 dogs in which at least 1 value was measured were not measured for NA (4%) and EHR score. Most dogs, particularly those born before 1990 or those from the Guiding Eyes for the Blind program, were not measured for the DI (73%) and DLS score (75%). Missing values were allowed in the multiple-trait model. A dog with a missing value for 1 hip joint trait was still assigned a predicted value for that trait on the basis of other available measurements and the same trait measured in its relatives. Therefore, a breeding value for all 4 hip joint traits could be estimated for a dog with no phenotype. Consequently, the breeding values of the DI and DLS score of any given dog could be inferred by the genetic correlation between the NAs and EHR scores of all its relatives without these 2 traits being measured. This is an important consideration given that hip joint radiographs are not available for some dogs in a pedigree from the semiopen OFA database, but their breeding value for a hip joint trait can still be estimated.

Thorough documentation of the pedigree would also improve the estimation of inbreeding coefficients and breeding values. Among 1,411 noninbred dogs in the present study, there were 552 dogs for which no parents were identified and 342 dogs with only 1 known parent. Nevertheless, because breeding values can be

estimated for dogs when no hip joint trait information is available, users of semiopen registries can still benefit from active participation because pedigree relationships allow breeding values for hip joints of nonparticipating dogs to be estimated.

When selecting dogs on the basis of breeding values for hip joint conformation, some consideration should be given to their inbreeding coefficients so genetic diversity is not adversely affected. Use of breeding values for hip joint conformation could lead to intensive use of dogs with good breeding values, thus narrowing genetic diversity. The effects of inbreeding would then accumulate at a higher rate. An efficient mating system would make use of predictions of the inbreeding coefficient that would result for progeny from mating a particular pair. Inbreeding coefficients for a potential breeding pair could be provided upon request simultaneously with breeding values to breeders and owners. A breeder may consider all available breeding values and calculate a selection index based on traits such as behavior, body size, and many orthopedic characteristics as long as they were measured and recorded. Each trait could be weighted for calculating the selection index on the basis of its importance to the breed organization. Given that mate pairing is also a factor in selective breeding, a male considered strong with respect to a trait could be paired with a female that is weak with respect to the same trait.

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