Housing- and exercise-related risk factors associated with the development of hip dysplasia as determined by radiographic evaluation in a prospective cohort of Newfoundlands, Labrador Retrievers, Leonbergers, and Irish Wolfhounds in Norway

Randi I. Krontveit, DVM; Ane Nødtvedt, DVM, PhD; Bente K. Sævik, DVM, PhD; Erik Ropstad, DVM, PhD; Cathrine Trangerud, DVM, PhD

Objective—To identify housing- and exercise-related risk factors associated with the development of hip dysplasia (HD) as determined by radiographic evaluation in Newfoundlands, Labrador Retrievers, Leonbergers, and Irish Wolfhounds in Norway.

Animals—501 client-owned dogs from 103 litters.

Procedures—Dogs were assessed from birth until official radiographic screening for HD at 12 (Labrador Retriever [n = 133] and Irish Wolfhound [63]) or 18 (Newfoundland [125] and Leonberger [180]) months of age. Information regarding housing and exercise conditions during the preweaning and postweaning periods was obtained with questionnaires. Multivariable random effects logistic regression models were used to identify housing- and exercise-related risk factors associated with the development of radiographically detectable HD.

Results—Puppies walking on stairs from birth to 3 months of age had an increased risk of developing HD. Factors associated with a decreased risk of developing HD included off-leash exercise from birth to 3 months of age, birth during the spring and summer, and birth on a farm. Significant clustering of dogs with HD was detected within litters.

Conclusions and Clinical Relevance—Results indicated that puppies ≤ 3 months old should not be allowed access to stairs, but should be allowed outdoor exercise on soft ground in moderately rough terrain to decrease the risk for developing radiographically detectable HD. These findings could be used as practical recommendations for the prevention of HD in Newfoundlands, Labrador Retrievers, Leonbergers, and Irish Wolfhounds. (*Am J Vet Res* 2012;73:838–846)

Hip dysplasia is an inherited developmental orthopedic disease in dogs.[1] Major genes and quantitative trait loci associated with HD have been identified via segregation analysis and molecular genetic analysis, respectively.[2,3] The expression of these genes might be influenced by environmental factors.[4] Although the etiopathogenesis of HD is not completely understood, 2 pathways have been proposed: coxofemoral (hip) joint laxity that results in hip joint instability and abnormal endochondral ossification that affects various joints, including the hip joints.[1,5,6] Hip joint instability in young puppies alters mechanical forces on the growing femoral head and acetabulum, which affects bone growth and remodeling and can result in joint deformity and osteoarthritis.[7,8] Edema and torn fibers of the ligament of the femoral head are the first observable changes associated with HD and have been detected in the hip joints of puppies as young as 30 days of age.[9,10]

The incidence of HD is unknown. Several dog breed registries in various countries have reported[11–15] the prevalence of HD for their respective breeds, which range from 2% to 67%. Large- and giant-breed dogs generally have a higher prevalence of HD than do smaller-breed dogs, although exceptions do exist.[16–20]

Abbreviations

HD	Hip dysplasia
ICC	Intraclass correlation coefficient
LRT	Likelihood ratio test

Received October 26, 2010.
Accepted June 9, 2011.
From the Departments of Companion Animal Clinical Sciences (Krontveit, Nødtvedt, Sævik, Trangerud) and Production Animal Clinical Sciences (Ropstad), Norwegian School of Veterinary Science, N-0033 Oslo, Norway.
Supported by grant No. 140541/110 from the Norwegian Research Council, the Norwegian School of Veterinary Science, and the Norwegian Kennel Club.
The authors thank Professor Jorunn Grøndalen, Professor Lars Moe, and Dr. Astrid Indrebø for assistance with initiation of the study and Professor Eystein Skjerve for technical assistance.
Address correspondence to Dr. Krontveit (randi.krontveit@nvh.no).

In a recent study[21] conducted in Norway, the incidence risk of HD in 4 kinds of large-breed dogs ranged from 10% in Irish Wolfhounds to 36% in Newfoundlands.

The Norwegian Kennel Club has a screening program for HD in certain breeds, which includes a standardized radiographic evaluation of hip joints at 12 or 18 months of age. For each dog screened, the HD status as determined via radiographic evaluation (radiographic HD) is recorded in a central registry. Investigators in multiple studies[22–28] that used information (individual dog pedigree and radiographic HD status) obtained from breed registries have reported moderate to high estimates for the heritability of HD. Various breed registries have tried to reduce the incidence of HD by requiring all registered dogs to be screened for HD via radiographic evaluation at a certain age and then imposing breeding restrictions on dogs with evidence of HD.[13,17,28–35] Several studies[12,13,19,20,36] have been conducted to evaluate the effect of selective breeding on the reduction of HD incidence and have yielded mixed and sometimes disappointing results for some breeds. Mixed linear regression models to predict the HD status of progeny of a prospective mating have been developed, and these models include variables for the HD phenotype of relatives of the sire and dam and may help improve the effectiveness of selective breeding for the reduction of HD incidence.[23,27,37]

Risk factors for HD that have been most commonly studied include those associated with a dog's growth rate, body size and conformation, and food consumption and the composition of the diet.[21,38–44] The development of HD has also been associated with estrogens and relaxin, which aid in the relaxation of the pelvic ligaments around parturition and are excreted in the milk of lactating bitches.[45–47] Results of 1 study[10] indicate that confinement of puppies predisposed to HD in small areas where activity was restricted decreased the risk of HD development, whereas results of another study[40] indicate that restricted activity of puppies did not influence HD development. Even though certain types of housing- and exercise-related variables have been associated with the development of HD,[48,49] to our knowledge, an extensive study of environmental risk factors associated with the development of HD in client-owned dogs managed under standard domestic conditions has not been performed.

The purpose of the study reported here was to identify housing- and exercise-related risk factors associated with the development of radiographic HD in 4 kinds (Newfoundland, Labrador Retriever, Leonberger, and Irish Wolfhound) of large-breed dogs. A cohort of client-owned dogs that were managed under standard domestic conditions was monitored prospectively from birth until radiographic screening for HD at 12 or 18 months of age. The hypothesis was that housing and exercise variables for growing dogs would be associated with an increased risk of developing HD. Results could then be used when making recommendations regarding housing and exercise for the prevention of HD in young puppies predisposed to developing HD.

Materials and Methods

Animals—The study reported here was part of a larger study (main study) designed to identify risk factors associated with the development of HD, elbow joint dysplasia, panosteitis, and osteosarcoma in Newfoundlands, Labrador Retrievers, Leonbergers, and Irish Wolfhounds. The sampling procedure and inclusion criteria for dogs included in the main study have been described.[21] Briefly, Newfoundland, Labrador Retriever, Leonberger, and Irish Wolfhound puppies born in Norway between November 1998 and June 2001 were eligible for inclusion in the main study. All puppies were registered with the Norwegian Kennel Club, and dogs from all geographic areas of Norway were included in the study. All dogs were client-owned animals, and the housing, exercise, and feeding regimen for each dog was determined by its breeder and subsequently its owner.

For the study reported here, a cohort of puppies from the main study was used to investigate environmental factors that may affect the development of HD in growing dogs. A total of 647 dogs from 106 litters (which represented 23.2% of the total litters of Newfoundland, Labrador Retriever, Leonberger, and Irish Wolfhound puppies born in Norway between November 1998 and June 2001) from the main study were considered for inclusion. To be included in the present study, each dog had to be officially screened for HD via radiographic evaluation, and a questionnaire regarding housing and exercise conditions had to be completed by the dog's owner at least once during the observation period, which was from birth to HD screening at 12 or 18 months of age. All dogs initially enrolled in the study did not continue until study completion. Reasons a dog was lost to follow-up included, but were not limited to, the death of the dog, relocation of the owner and dog, and exportation of the dog.[21,a] Information for 501 dogs from 103 litters was included in the study reported here.

The present study was performed in accordance with provisions established and enforced by the National Animal Research Authority of Norway. Each breeder, dog owner, and veterinarian associated with dogs included in the present study signed an agreement of cooperation to comply with the study plan.

Radiographic screening for HD—For each dog in the present study, radiographic screening for HD was conducted in accordance with standards established by the Fédération Cynologique Internationale at the age recommended by the Norwegian Kennel Club for each breed. Thus, Labrador Retrievers and Irish Wolfhounds underwent radiographic evaluation at 12 months of age, and Newfoundlands and Leonbergers underwent radiographic evaluation at 18 months of age. Each dog was sedated to achieve complete muscle relaxation and then was positioned in dorsal recumbency with the hind limbs extended and abducted such that the patellae were superimposed over the femora. The pelvis, femora, and patellae were included on each radiographic image, and images were obtained at a film-to-focus distance of 100 cm. Each radiograph was uniquely identified with the dog's Norwegian Kennel Club registration, tattoo, or microchip number and was then developed.

All radiographic images were sent to the respective national kennel club in the country where the dog resided for evaluation by an experienced veterinary radiologist. Greater than 90% of the radiographs were evaluated by a veterinary radiologist at the Norwegian Kennel Club. However, some of the dogs had been relocated to Sweden or Denmark; therefore, radiographs for those dogs were evaluated by an experienced veterinary radiologist at the Swedish Kennel Club or Danish Kennel Club, respectively. For all dogs, the Fédération Cynologique Internationale 5-class grading scale was used to classify hip joints: A (excellent), B (normal), C (mild dysplasia), D (moderate dysplasia), and E (severe dysplasia). The HD grades are defined descriptively on the basis of the size of the Norberg angle, degree of subluxation of the hip joint, shape and depth of the acetabulum, and radiographic evidence of secondary joint disease.[50] For each dog, each hip joint was classified separately, and the final classification for a dog was that of the most severely affected hip joint. Dogs that had a final hip joint classification of C, D, or E were considered affected with HD.

Questionnaires—For each dog, housing and exercise information was obtained by the use of written questionnaires[b] that were administered to the breeder of the litter and the owner of the dog. The questionnaires were bound into a booklet, and each sheet of the booklet had a carbonless copy so that 1 copy could be mailed to the investigators at the appointed times and 1 copy was retained within the booklet. There was 1 booklet for the breeder and 1 booklet for the owner. The questionnaires consisted of open- and closed-ended (multiple choice) questions. Breeders were responsible for providing information about dogs from birth until weaning (approx 8 weeks of age); information obtained included dog identification, date of birth, breed, sex, litter size, region where birth took place, type of housing (single-family home or farm), type of bedding in whelping box, type of surfaces to which puppies were exposed indoors and outdoors, and whether dogs were exposed to snow and ice. Owners were responsible for providing information about dogs at 3, 4, 6, and 12 months of age; information obtained included region where a dog resided, type of housing (single-family home, farm, or apartment building), presence of children and other animals in the household, type of surfaces to which dogs were exposed indoors and outdoors, whether dogs were exposed to snow and ice, and amount and type of daily exercise. Preliminary analyses revealed bias in the owners' recording regarding exercise. The exercise variables were therefore reclassified from categorical to dichotomous variables.

Risk factor analysis—Commercially available software[c] was used for all analyses. Data obtained from the questionnaires were separated into 1 of 3 categories: preweaning variables, postweaning housing-related variables, and postweaning exercise-related variables. A complete list of the variables obtained from the questionnaires and used in statistical modeling was compiled (**Appendix**). To evaluate the association of weather conditions during the preweaning period with the development of HD, season of birth was evaluated via 2 different categorizations: meteorologic[51,52] (in which winter was defined as December through March, spring was defined as April through May, summer was defined as June through August, and fall was defined as September through November) and calendar (in which each season consisted of 3 months; thus, March was included in spring instead of winter). However, the meteorologic categorization for season of birth was the a priori categorization chosen for season of birth, and the meteorologic categorization for season of birth was used for all multivariable analyses.

Because of the large number of variables that were considered at each time (0 to 8 weeks and 3, 4, 6, and 12 months of age), the data were analyzed separately at each time to identify key variables that were then considered in a final multivariable model.[53,54] The outcome of interest, or dependent variable, for all models was HD status; dogs that were assigned a hip joint grade A or B on radiographic evaluation were classified as HD free, and those that were assigned a hip joint grade of C, D, or E were classified as HD affected. Given that the dependent variable was dichotomous, a mixed logistic regression model was used to determine risk factors that were associated with HD-affected dogs. Because study dogs were clustered in litters, litter was included in all models as a random effect.

For each respective time, univariable logistic regression models were considered for each independent variable. Independent variables that had a Wald χ^2 value of $P < 0.20$ on univariable analysis were eligible for consideration in multivariable models. Before multivariable models were constructed, collinearity between independent variables was evaluated by the use of a Goodman and Kruskal γ for dichotomous and ordinal variables and a phi coefficient for nominal variables. Collinearity was considered to exist if r was ≥ 0.7 or ≤ -0.7. When collinearity was detected between 2 independent variables, the variable with the least amount of missing data was selected for further analyses. Also, variables that had missing values for > 20% of the observations were not considered in multivariable analyses.

Multivariable logistic regression models were initially constructed by backward elimination. Additionally, a causal diagram was created as an aid for evaluation of potential confounding and intervening variables. On the causal diagram, a confounding or intervening variable was one that was included on the causal pathway between another independent variable and the dependent variable. A variable was differentiated as a confounding or intervening variable on the basis of the magnitude of change in the regression coefficients and the significance of the effects for other independent variables in models with and without the confounding or intervening variable of interest. A confounding variable was defined as a variable that resulted in a change of > 20% in the regression coefficient of at least 1 other independent variable in the model. An intervening variable was defined as a variable that eliminated the effect (Wald χ^2 value of $P \geq 0.05$) of at least 1 other variable in the model. Once identified, intervening variables were eliminated from further multivariable regression analyses. During that initial phase of multivariable model construction, only those variables with a Wald χ^2 value of $P < 0.05$ were retained.

Following the initial phase of multivariable logistic regression model construction, all possible interactions among the remaining independent variables were considered in the model. Interactions were maintained in the model only if the LRT for the comparison of the full model (model containing the interaction term) with the reduced model (model without the interaction term) had a value of $P < 0.01$.

Once interaction terms were identified, independent variables that had been eliminated but were not classified as intervening variables were forced back into the multivariable model 1 at a time. Only variables with a Wald χ^2 $P < 0.05$ were retained in the final multivariable model at each time point.

The significance of the random effect of litter was evaluated by means of an LRT that compared a multivariable model that included litter as a random effect with a multivariable model that did not include litter as a random effect, but which otherwise contained the same fixed effects. The random effect of litter was considered significant if the 1-sided LRT had a value of $P \leq 0.05$.

For all time points combined, a final multivariable model was constructed in a manner similar to that for each individual time point, except only variables that were found to have a significant effect at each respective time point were considered. From that model, the between-litter variance was calculated via a latent variable approach[53] with the assumption that dog-level variance was constant at $\pi^2/3$ such that ICC = $\sigma^2_{litter}/(\sigma^2 + \sigma^2_{litter})$, where σ^2_{litter} is the between-litter variance and σ^2 is the dog-level variance. To evaluate the goodness of fit of the final multivariable model, residuals were estimated for individual dogs as well as for litters. Litter-level residuals were plotted against predicted and fitted values to assess the assumptions of homoscedasticity and normality.[53] Also, model fit was evaluated for multivariable regression models with and without breed and season of birth by means of a Wald test and LRT.

Results

Animals—A total of 501 of 647 (77%) dogs from 103 litters were officially screened for HD and had a housing and exercise questionnaire completed at least once during the period from birth until 12 months of age. The 103 litters were the offspring of 94 dams owned by 86 breeders. The most common reasons that a dog was not screened for HD (n = 146) were death of the dog and unwillingness of the owner to pay for the radiographic evaluation. The distribution of dogs among breeds was 125 Newfoundlands, 133 Labrador Retrievers, 180 Leonbergers, and 63 Irish Wolfhounds. On the basis of radiographic evaluation, 123 (24.6%) dogs were classified as HD affected (received a hip joint grade of C, D, or E). The distribution of HD-free and HD-affected dogs by breed was summarized (**Table 1**). The radiographs for the majority (n = 491) of dogs were evaluated by a veterinary radiologist for the Norwegian Kennel Club; radiographs for 8 dogs were evaluated by a veterinary radiologist for the Swedish Kennel Club, and radiographs for 2 dogs were evaluated by a veterinary radiologist for the Danish Kennel Club.

Questionnaires—A total of 457 questionnaires regarding preweaning housing and exercise conditions were returned by the breeders to the study investigators, whereas owners returned 478, 460, 443, and 397 questionnaires at 3, 4, 6, and 12 months, respectively. Unfortunately, not all questions on the questionnaires were answered at each time point; therefore, the number of responses differed among variables.

Risk factors—Breed and litter size were included in all multivariable models to control for differences in litter size among the breeds. No collinearity was detected between any of the variables, and none of the interaction terms were found to have a significant association with the development of HD.

Variables during the preweaning period (birth to 8 weeks of age) that had a significant association with development of HD included breed, season of birth, and type of housing (single-family home or farm). Variables during the period from weaning to 3 months of age that had a significant association with HD included breed, exercise in a run with a soft surface (ground or grass), daily use of stairs, and off-leash exercise in a park-like terrain. The final multivariable regression model included breed, litter size, type of housing (single-family home or farm) at the breeder, daily use of stairs from weaning to 3 months of age, and daily off-leash exercise in a park-like terrain from weaning to 3 months of age (**Table 2**). Significant clustering of HD-affected dogs within litters (ICC, 0.183; $P = 0.006$) was also detected. Goodness of fit for the final overall multivariable regression model was deemed to be adequate because the assumptions of homoscedasticity and normality were met as determined by evaluation of litter-level residuals, and no extreme residual values were detected at the dog level.

The Wald test and LRT were performed to compare multivariable models with and without breed and season of birth, and the results of both tests were significant, which suggested that breed and season of birth were important factors in the development of HD. To evaluate the effect of the classification system used for season of birth, the categorization of season of birth was changed such that winter was defined as December through February, spring was defined as March through May, summer was defined as June through August, and fall was defined as September through November. With

Table 1—Number (percentage) of dogs classified as HD free and HD affected on the basis of radiographic evaluation at 12 (Labrador Retriever and Irish Wolfhound) or 18 (Newfoundland and Leonberger) months of age in a cohort of 501 dogs in Norway.

Breed	HD free	HD affected	Total dogs tested
Newfoundland	80 (64.0)	45 (36.0)	125
Labrador Retriever	106 (79.7)	27 (20.3)	133
Leonberger	135 (75.0)	45 (25.0)	180
Irish Wolfhound	57 (90.5)	6 (9.5)	63

The Fédération Cynologique Internationale grading scale was used to classify the hip joint status of the dogs: A (excellent), B (normal), C (mild dysplasia), D (moderate dysplasia), and E (severe dysplasia). For each dog, each hip joint was graded separately, and the dog was classified as HD free (grades A and B) or HD affected (grades C, D, and E) on the basis of the most severe hip joint grade.

Table 2—Final multivariable random effects logistic regression model for determining the association of housing- and exercise-related risk factors with HD (as determined by radiographic evaluation) in a cohort of 501 large-breed dogs in Norway.

Variable	OR	95% confidence interval	*P* value
Breed			
Newfoundland	Referent	—	—
Labrador Retriever	0.26	0.10–0.66	0.005
Leonberger	0.59	0.26–1.36	0.213
Irish Wolfhound	0.16	0.05–0.58	0.005
Litter size	0.91	0.79–1.04	0.170
Season of birth*			
Winter	Referent	—	—
Spring	0.54	0.21–1.36	0.188
Summer	0.62	0.25–1.54	0.303
Fall	2.13	0.92–4.96	0.078
Type of housing at breeder			
Single-family home (urban or suburban)	Referent	—	—
Farm (rural area)	0.34	0.15–0.78	0.010
Daily use of stairs from birth until 3 months of age	1.96	1.14–3.35	0.015
Daily off-leash exercise in park from birth until 3 months of age	0.31	0.15–0.65	0.002
Overall *P* value (final model)†	—	—	< 0.001

The LRT for the random litter effect was significant (ICC = 0.183; $P = 0.006$).

*Season of birth was categorized as follows: winter, December through March; spring, April through May; summer, June through August; and fall, September through November. †Final model had a β_0 of 0.810.

— = Not applicable.

See Table 1 for remainder of key.

this categorization for season of birth and winter used as the referent group, the odds of a dog being classified as HD affected were 1.3, 0.9, and 3.2 if it was born during the spring, summer, and fall, respectively.

Discussion

In the present study, dogs born during the winter (December through March) and fall (September through November) and that used stairs daily during the period from weaning to 3 months of age had an increased risk for developing radiographic HD. In contrast, dogs that were born during spring (April through May) and summer (June through August) and spent their preweaning period on a farm and were allowed off-leash exercise in a park-like terrain during the period from weaning to 3 months of age had a decreased risk for developing radiographic HD. These findings supported our hypothesis that housing and exercise conditions for growing large-breed dogs affect the development of HD. There was also significant clustering of HD-affected dogs within litters, which indicated that heredity as well as housing and exercise conditions affects HD development.

For the study reported here, exercise-related variables were associated with radiographic HD development, but only during the period from weaning until 3 months of age. Investigators in 1 study[10] recommended that puppies predisposed to developing HD be confined in a cage to restrict exercise. Confinement in a small area increases the amount of time a puppy spends in a sitting position, which maintains an abduction-flexion position in the hip joint and supports a forced hip joint congruence.[10] However, confinement is not currently recommended for the prevention of HD because puppies will not develop socially,[4] and it is not practicable for most breeders. Moreover, restricted exercise of growing puppies was not associated with the development of HD in another study.[40]

Results of a retrospective case-control study[48] of adult Labrador Retrievers (12 to 24 months old) with known radiographic HD status indicated that regular exercise by running after a ball or stick thrown by the owner increases the risk of developing HD. The protective effect of off-leash exercise for puppies ≤ 3 months old in the present study might indicate increased muscle development and strength in the hip area. Dogs with high pelvic muscle mass are more likely to have normal development of the hip joints.[55,56] Results of kinematic analysis studies[57,58] of healthy adult dogs indicated that controlled descent on stairs and walking uphill improve flexion and range of motion of the hip joints and thus are beneficial therapeutic exercises for dogs with musculoskeletal disorders affecting the pelvic limbs. Investigators who conducted a kinematic study[59] of puppies with hip joint laxity reported gait inconsistencies that they suspected were caused by a lack of development of neuromuscular function and coordination. Underdevelopment of neuromuscular function and coordination may explain the increased risk of HD development in puppies that walked up and down stairs daily from weaning to 3 months of age. However, the frequency with which dogs climb stairs and the rates of ascent and descent might also influence that association and should be studied further. Some exercise-related activities in the present study (ie, running alongside a moving bike and running after balls or sticks thrown by the owner) were not commonly performed, which may have resulted in an insufficient number of observations for those particular variables for the detection of a significant association with the development radiographic HD.

In the present study, exercise-related variables for dogs > 3 months old were not associated with an increased risk of developing radiographic HD. In foals, results of studies[60,61] indicate that the first months after birth was the period during which the musculoskeletal system was most vulnerable to injury and the development of orthopedic disease. Rapid growth and development might make the musculoskeletal apparatus more susceptible to environmental influences. In the cohort of large-breed dogs in the present study, average daily weight gain peaked at approximately 3 months of age.[21,62] In dogs, hip joints are typically normal at birth, and the most critical time for the development and stability of the hip joint is from birth to 60 days of age.[9,10] Therefore, the beneficial and negative effects of various kinds of exercise might be most pronounced during this time. The cohort of dogs used in the present study will be studied further to evaluate the effect of various exercise conditions soon after birth on the development of clinical signs of HD and long-term survival.

The only housing-related variable that was retained in the final multivariable regression model was the type of housing at the breeder. If puppies were born on a farm or in a rural area, the risk of HD was decreased (OR, 0.34), compared with that for puppies born in a single-family home in an urban or suburban area. The most probable explanation for this association is that puppies born in rural areas have more opportunities for unrestricted exercise outside than those born in urban or suburban areas. Box stall rest and irregular exercise were associated with increased severity of osteochondrosis lesions in foals.[60] In regard to HD development in dogs, housing conditions have not been extensively studied, but exposure to a slippery floor surface prior to weaning increased the risk of developing clinical signs of HD in a cohort of Boxers.[49] In the study reported here, none of the variables related to resting or indoor or outdoor floor surfaces were associated with HD development. However, the HD status in the present study was determined by radiographic evaluation of the hip joints, whereas that of the other study[49] was determined by the presence of clinical signs of HD.

In the present study, dogs born in the fall had twice the risk of developing HD, compared with that for dogs born in the winter. For dogs that were born during the spring and summer, the risk of being classified as HD affected was approximately half that of dogs born during the winter. Other studies[37,63–65] have found similar associations between season of birth and HD. A possible explanation for the observed seasonal effect is that housing and exercise conditions change with the season, such that puppies born during the spring and summer get more unrestricted exercise on soft ground than puppies born in the fall and winter. This may have a beneficial impact on muscle development and strength, although other unmeasured variables may have altered or biased our results. For the analysis in which puppies born during March were classified as being born in the winter, the protective effect of spring was lost (OR, 1.3), and the risk of developing HD among dogs born during the fall increased (OR, 3.2). By meteorologic definition, spring begins when night temperatures are > 0°C for 7 consecutive nights; therefore, March is a winter month in most parts of Norway.[51,52] Including dogs born in March in the spring category diminished the difference in the odds of being classified as HD affected between dogs born in the winter and spring and provided support for the hypothesis that the effect of season of birth on HD is mediated by outdoor climate and dogs exercising less during winter months.

In the study reported here, there was significant clustering (ICC, 18.3%) of dogs affected with HD within litters, which indicated that HD had genetic components and some other litter-related components that were not measured. The magnitude of clustering was similar to that (22.6%) calculated in another study[21] in which investigators evaluated growth-related risk factors for HD in the same cohort of dogs used in the present study. In a study[66] conducted to evaluate the association of preweaning mortality rate in puppies with additive genetic, between-litter, and within-litter factors, litter factors were responsible for most of the variation.

The results of the present study may have been affected by interpretation of hip joint radiographs that resulted in misclassification of dogs as HD free or HD affected. The evaluation of conventional radiographs of hip joints to diagnose HD may result in a false-negative diagnosis; whereas evaluation of distraction index radiographs of hip joints may result in a false-positive diagnosis of HD.[67] Most of the radiographs in the present study were evaluated by 1 radiologist; thus, interobserver variation and misclassification should have been minimized.[68] Also, consolidating the hip joint status of dogs into 2 categories (HD free and HD affected) from the 5-class grading scale reduced variation and resulted in some loss of information. Results of radiographic screening for HD are affected by the age of the dog at the time of screening. Secondary changes in the hip joint are more likely to become evident over time; therefore, older dogs generally receive more severe grades than do younger dogs.[22,28,37,69] In the present study, the fact that Newfoundlands and Leonbergers were 6 months older at screening than were Labrador Retrievers and Irish Wolfhounds may have been a source of differential misclassification.

Selection bias would have been possible if the dogs not screened for HD and excluded from the present study were more or less likely to be affected by HD. However, the 2 primary reasons for dogs being excluded from the study were death of the dog and the owner's unwillingness to pay for the radiographic evaluation. It seems unlikely that either of those reasons would be associated with a dog's HD status.

In the study reported here, there were a number of missing observations for some of the variables, which may have reduced the power to detect potential associations with HD, particularly at the older ages. Reclassification of exercise variables from categorical to dichotomous variables also resulted in some loss of information, although it likely reduced information bias from the questionnaires. When large numbers of variables are investigated, a variable might have a significant effect by chance alone. In the present study, efforts to reduce the number of independent variables were made by selecting variables on the basis of a causal diagram, considering variables that had liberal *P* values ($P \leq 0.20$) on univariable analyses eligible for multivariable analyses, and then building multivariable models by use of logical subsets of variables (from the preweaning period and the different observational ages) to identify key variables at each time.[53,54] These key variables were then retained for consideration in the final multivariable model.

Cohort studies are generally considered to have high external validity.[53] Most studies conducted to investigate the development of HD have been controlled studies or performed in populations of dogs preselected for certain purposes (eg, guide dogs). In such studies, dogs are often the offspring of parents with HD and are raised in kennels where feeding, exercise, and housing regimens are controlled and standardized and are not representative of client-owned dogs that have more diverse husbandry. The present study was a large-scale prospective cohort study in which dogs used for breeding purposes as well as dogs maintained only as pets were included. Therefore, the results should be externally valid for the 4 kinds of large-breed dogs studied in Norway and perhaps for large-breed dogs with similar husbandry in other countries.

In the study reported here, type of housing, exercise conditions, and season of birth were significantly associated with the risk of an HD diagnosis at radiographic screening in a cohort of large-breed dogs. However, the effects of these risk factors were limited to the first 3 months after birth. Thus, efforts to prevent the development of HD via housing and exercise should be initiated early in a puppy's life. Results indicated that puppies ≤ 3 months old should not be allowed access to stairs, but should be allowed outdoor exercise on soft ground in moderately rough terrain to decrease the risk for developing HD. Unfortunately, a recommendation on the amount of exercise could not be made because it was not analyzed in the present study.

a. Trangerud C. *Growth patterns and metaphyseal irregularities in dogs: a study of 4 large breeds with emphasis on irregularities in the distal metaphysis of the radius and ulna*. PhD thesis, Norwegian School of Veterinary Science, Oslo, Norway, 2008.
b. A booklet containing the questionnaires is available from the corresponding author upon request. Questionnaires are written in Norwegian.
c. Stata, version 11, Stata Corp, College Station, Tex.

References

1. Todhunter RJ, Lust G. Hip dysplasia: pathogenesis. In: Slatter D, ed. *Textbook of small animal surgery*. 3rd ed. Philadelphia: WB Saunders Co, 2003;2009–2019.
2. Mäki K, Janss LL, Groen AF, et al. An indication of major genes affecting hip and elbow dysplasia in four Finnish dog populations. *Heredity* 2004;92:402–408.
3. Todhunter RJ, Mateescu R, Lust G, et al. Quantitative trait loci for hip dysplasia in a cross-breed canine pedigree. *Mamm Genome* 2005;16:720–730.
4. Ginja MM, Silvestre AM, Gonzalo-Orden JM, et al. Diagnosis, genetic control and preventive management of canine hip dysplasia: a review. *Vet J* 2010;184:269–276.
5. Madsen JS. The joint capsule and joint laxity in dogs with hip dysplasia. *J Am Vet Med Assoc* 1997;210:1463–1465.
6. Todhunter RJ, Zachos TA, Gilbert RO, et al. Onset of epiphyseal mineralization and growth plate closure in radiographically normal and dysplastic Labrador Retrievers. *J Am Vet Med Assoc* 1997;210:1458–1462.
7. Weigel JP, Wasserman JF. Biomechanics of the normal and abnormal hip joint. *Vet Clin North Am Small Anim Pract* 1992;22:513–528.
8. Fries CL, Remedios AM. The pathogenesis and diagnosis of canine hip dysplasia: a review. *Can Vet J* 1995;36:494–502.
9. Alexander JW. The pathogenesis of canine hip dysplasia. *Vet Clin North Am Small Anim Pract* 1992;22:503–511.
10. Riser WH. The dog as a model for the study of hip dysplasia. Growth, form, and development of the normal and dysplastic hip joint. *Vet Pathol* 1975;12:234–334.
11. Genevois JP, Remy D, Viguier E, et al. Prevalence of hip dysplasia according to official radiographic screening, among 31 breeds of dogs in France. *Vet Comp Orthop Traumatol* 2008;21:21–24.
12. Kaneene JB, Mostosky UV, Miller R. Update of a retrospective cohort study of changes in hip joint phenotype of dogs evaluated by the OFA in the United States, 1989–2003. *Vet Surg* 2009;38:398–405.
13. Leppänen M, Saloniemi H. Controlling canine hip dysplasia in Finland. *Prev Vet Med* 1999;42:121–131.
14. Paster ER, LaFond E, Biery DN, et al. Estimates of prevalence of hip dysplasia in Golden Retrievers and Rottweilers and the influence of bias on published prevalence figures. *J Am Vet Med Assoc* 2005;226:387–392.
15. Smith GK. Advances in diagnosing canine hip dysplasia. *J Am Vet Med Assoc* 1997;210:1451–1457.
16. LaFond E, Breur GJ, Austin CC. Breed susceptibility for developmental orthopedic diseases in dogs. *J Am Anim Hosp Assoc* 2002;38:467–477.
17. Corley EA, Hogan PM. Trends in hip dysplasia control: analysis of radiographs submitted to the Orthopedic Foundation for Animals, 1974 to 1984. *J Am Vet Med Assoc* 1985;187:805–809.
18. Priester WA, Mulvihill JJ. Canine hip dysplasia: relative risk by sex, size, and breed, and comparative aspects. *J Am Vet Med Assoc* 1972;160:735–739.
19. Lingaas F, Heim P. Genetic investigation on hip dysplasia in Norwegian dog breeds. *Nor Vet Tids* 1987;99:617–623.
20. Flückiger M, Lang J, Binder H, et al. The control of hip dysplasia in Switzerland. A retrospect of the past 24 years. *Schweiz Arch Tierheilkd* 1995;137:243–250.
21. Krontveit RI, Nødtvedt A, Sævik BK, et al. A prospective study on canine hip dysplasia and growth in a cohort of four large breeds in Norway (1998–2001). *Prev Vet Med* 2010;97:252–263.
22. Mäki K, Liinamo AE, Ojala M. Estimates of genetic parameters for hip and elbow dysplasia in Finnish Rottweilers. *J Anim Sci* 2000;78:1141–1148.
23. Malm S, Fikse WF, Danell B, et al. Genetic variation and genetic trends in hip and elbow dysplasia in Swedish Rottweiler and Bernese Mountain Dog. *J Anim Breed Genet* 2008;125:403–412.
24. Engler J, Hamann H, Distl O. Estimation of genetic parameters for radiographic signs of hip dysplasia in Labrador Retrievers. *Berl Munch Tierarztl Wochenschr* 2008;121:359–364.
25. Hedhammar A, Olsson SE, Andersson SA, et al. Canine hip dysplasia: study of heritability in 401 litters of German Shepherd Dogs. *J Am Vet Med Assoc* 1979;174:1012–1016.
26. Janutta V, Distl O. Inheritance of canine hip dysplasia: review of estimation methods and of heritability estimates and prospects on further developments. *Dtsch Tierarztl Wochenschr* 2006;113:6–12.
27. Madsen P. Index for HD. Available at: www.nkk.no/nkk/public/getAttachment?ATTACHMENT_ID=3751&ARTICLE_ID=3750. Accessed Jun 2, 2009.
28. Swenson L, Audell L, Hedhammar A. Prevalence and inheritance of and selection for hip dysplasia in seven breeds of dogs in Sweden and benefit: cost analysis of a screening and control program. *J Am Vet Med Assoc* 1997;210:207–214.
29. Janutta V, Hamann H, Distl O. Genetic and phenotypic trends in canine hip dysplasia in the German population of German Shepherd Dogs. *Berl Munch Tierarztl Wochenschr* 2008;121:102–109.
30. Lingaas F, Klemetsdal G. Breeding values and genetic trend for hip dysplasia in the Norwegian Golden Retriever population. *J Anim Breed Genet* 1990;107:437–443.
31. Willis MB. A review of the progress in canine hip dysplasia control in Britain. *J Am Vet Med Assoc* 1997;210:1480–1482.
32. Heim P. Screening for hip dysplasia in Norway, in *Proceedings*. Federation Eur Companion Anim Vet Assoc Contin Educ Course Aspects Arthrol 1999;40–44.
33. Adams WM. Radiographic diagnosis of hip dysplasia in the young dog. *Vet Clin North Am Small Anim Pract* 2000;30:267–280.
34. Adams WM, Dueland RT, Daniels R, et al. Comparison of two palpation, four radiographic and three ultrasound methods for early detection of mild to moderate canine hip dysplasia. *Vet Radiol Ultrasound* 2000;41:484–490.
35. Dassler CL. Canine hip dysplasia: diagnosis and nonsurgical treatment. In: Slatter D, ed. *Textbook of small animal surgery*. 3rd ed. Philadelphia: WB Saunders Co, 2003;2019–2029.
36. Hou Y, Wang Y, Lust G, et al. Retrospective analysis for genetic improvement of hip joints of cohort Labrador Retrievers in the United States: 1970–2007. *PLoS ONE* [serial online] 2010;5:e9410. Available at: www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0009410. Accessed May 5, 2010.
37. Leppänen M, Mäki K, Juga J, et al. Factors affecting hip dysplasia in German Shepherd Dogs in Finland: efficacy of the current improvement programme. *J Small Anim Pract* 2000;41:19–23.
38. Kasström H. Nutrition, weight gain and development of hip dysplasia. An experimental investigation in growing dogs with special reference to the effect of feeding intensity. *Acta Radiol Suppl* 1975;344:135–179.
39. Kealy RD, Olsson SE, Monti KL, et al. Effects of limited food consumption on the incidence of hip dysplasia in growing dogs. *J Am Vet Med Assoc* 1992;201:857–863.

40. Lust G, Geary JC, Sheffy BE. Development of hip dysplasia in dogs. *Am J Vet Res* 1973;34:87–91.
41. Lopez MJ, Quinn MM, Markel MD. Associations between canine juvenile weight gain and coxofemoral joint laxity at 16 weeks of age. *Vet Surg* 2006;35:214–218.
42. Richardson DC. The role of nutrition in canine hip dysplasia. *Vet Clin North Am Small Anim Pract* 1992;22:529–540.
43. Comhaire FH, Snaps F. Comparison of two canine registry databases on the prevalence of hip dysplasia by breed and the relationship of dysplasia with body weight and height. *Am J Vet Res* 2008;69:330–333.
44. Roberts T, McGreevy PD. Selection for breed-specific long-bodied phenotypes is associated with increased expression of canine hip dysplasia. *Vet J* 2010;183:266–272.
45. Goldsmith LT, Lust G, Steinetz BG. Transmission of relaxin from lactating bitches to their offspring via suckling. *Biol Reprod* 1994;50:258–265.
46. Kasström H, Aakvaag A, Edqvist LE, et al. Plasma levels of estradiol and plasma protein binding of sex steroids in dogs. An investigation with special reference to development of hip dysplasia in growing individuals. *Acta Radiol Suppl* 1975;344:121–133.
47. Steinetz BG, Williams AJ, Lust G, et al. Transmission of relaxin and estrogens to suckling canine pups via milk and possible association with hip joint laxity. *Am J Vet Res* 2008;69:59–67.
48. Sallander MH, Hedhammar A, Trogen ME. Diet, exercise, and weight as risk factors in hip dysplasia and elbow arthrosis in Labrador Retrievers. *J Nutr* 2006;136:2050S–2052S.
49. van Hagen MA, Ducro BJ, van den Broek J, et al. Incidence, risk factors, and heritability estimates of hind limb lameness caused by hip dysplasia in a birth cohort of Boxers. *Am J Vet Res* 2005;66:307–312.
50. Flückiger M. Scoring radiographs for canine hip dysplasia—the big three organisations in the world. *Eur J Companion Anim Pract* 2007;17:135–140.
51. Norwegian Meteorological Institute. Weather forecasts for Norway and the world. Available at: www.yr.no/nyheter/1.7521560. Accessed May 28, 2011.
52. Swedish Meteorological and Hydrological Institute. Meteorologi. Available at: www.smhi.se/kunskapsbanken/meteorologi/var-1.1080. Accessed Apr 5, 2011.
53. Dohoo I, Martin W, Stryhn H. Chapters 12–22. In: McPike SM, ed. *Veterinary epidemiologic research*. 2nd ed. Charlottestown, PE, Canada: VER Inc, 2009;243–603.
54. Lofstedt J, Dohoo IR, Duizer G. Model to predict septicemia in diarrheic calves. *J Vet Intern Med* 1999;13:81–88.
55. Cardinet GH III, Kass PH, Wallace LJ, et al. Association between pelvic muscle mass and canine hip dysplasia. *J Am Vet Med Assoc* 1997;210:1466–1473.
56. Riser WH, Shirer JF. Correlation between canine hip dysplasia and pelvic muscle mass: a study of 95 dogs. *Am J Vet Res* 1967;28:769–777.
57. Millard RP, Headrick JF, Millis DL. Kinematic analysis of the pelvic limbs of healthy dogs during stair and decline slope walking. *J Small Anim Pract* 2010;51:419–422.
58. Holler PJ, Brazda V, Dal-Bianco B, et al. Kinematic motion analysis of the joints of the forelimbs and hind limbs of dogs during walking exercise regimens. *Am J Vet Res* 2010;71:734–740.
59. Lopez MJ, Quinn MM, Markel MD. Evaluation of gait kinetics in puppies with coxofemoral joint laxity. *Am J Vet Res* 2006;67:236–241.
60. Barneveld A, van Weeren PR. Conclusions regarding the influence of exercise on the development of the equine musculoskeletal system with special reference to osteochondrosis. *Equine Vet J Suppl* 1999;(31):112–119.
61. Lepeule J, Bareille N, Robert C, et al. Association of growth, feeding practices and exercise conditions with the prevalence of developmental orthopaedic disease in limbs of French foals at weaning. *Prev Vet Med* 2009;89:167–177.
62. Trangerud C, Grøndalen J, Indrebø A, et al. A longitudinal study on growth and growth variables in dogs of four large breeds raised in domestic environments. *J Anim Sci* 2007;85:76–83.
63. Hanssen I. Hip dysplasia in dogs in relation to their month of birth. *Vet Rec* 1991;128:425–426.
64. Ohlerth S, Lang J, Busato A, et al. Estimation of genetic population variables for six radiographic criteria of hip dysplasia in a colony of Labrador Retrievers. *Am J Vet Res* 2001;62:846–852.
65. Wood JL, Lakhani KH. Effect of month of birth on hip dysplasia in Labrador Retrievers and Gordon Setters. *Vet Rec* 2003;152:69–72.
66. van der Beek S, Nielen AL, Schukken YH, et al. Evaluation of genetic, common-litter, and within-litter effects on preweaning mortality in a birth cohort of puppies. *Am J Vet Res* 1999;60:1106–1110.
67. Zhu L, Zhang Z, Friedenberg S, et al. The long (and winding) road to gene discovery for canine hip dysplasia. *Vet J* 2009;181:97–110.
68. Verhoeven GE, Coopman F, Duchateau L, et al. Interobserver agreement on the assessability of standard ventrodorsal hip-extended radiographs and its effect on agreement in the diagnosis of canine hip dysplasia and on routine FCI scoring. *Vet Radiol Ultrasound* 2009;50:259–263.
69. Wood JL, Lakhani KH. Hip dysplasia in Labrador Retrievers: the effects of age at scoring. *Vet Rec* 2003;152:37–40.

Appendix appears on the next page

Appendix

List of variables used for statistical modeling of the association of housing- and exercise-related risk factors with HD (as determined via radiographic evaluation) in a cohort of 501 large-breed dogs in Norway.

Variable	Type of data
Preweaning variables (information obtained from breeder during period from birth to 8 wk of age)	
Breed (Newfoundland, Labrador Retriever, Leonberger, or Irish Wolfhound)	Categorical
Sex (male or female)	Categorical
Litter size	Continuous
Season of birth (categorized on the basis of meteorologic definitions of seasons and determined by month in which a puppy was born): winter (December through March), spring (April through May), summer (June through August), fall (September through November)	Categorical
Type of community of birth (country, city, or suburban)	Categorical
Type of housing (single-family home [urban or suburban] or farm [rural area])	Categorical
Padding in whelping box	
Newspaper (yes or no)	Dichotomous
Sawdust (yes or no)	Dichotomous
Carpet (yes or no)	Dichotomous
Inside environment	
Parquet or wood (yes or no)	Dichotomous
Linoleum (yes or no)	Dichotomous
Carpet (yes or no)	Dichotomous
Tile (yes or no)	Dichotomous
Outside environment	
Soft (grass, dirt, and gravel [yes or no])	Dichotomous
Hard (wood, asphalt, and concrete [yes or no])	Dichotomous
Snow and ice (yes or no)	Dichotomous
Postweaning housing variables (information obtained from owner at 3, 4, 6, and 12 mo of age)	
Type of community of residence (country, suburban, or city)	Categorical
Type of housing (single-family home [urban or suburban], farm [rural area], or apartment building)	Categorical
Were children in the household? (yes or no)	Dichotomous
Were other dogs in the household? (yes or no)	Dichotomous
Inside resting surface	
Soft: bed, mattress, pillow, quilt, and sofa (yes or no)	Dichotomous
Hard: wood, parquet, linoleum, tile, concrete, or thin carpet (yes or no)	Dichotomous
Outside resting surface	
Soft: grass, dirt or sand (yes or no)	Dichotomous
Hard: wood, asphalt, concrete, or gravel (yes or no)	Dichotomous
Snow and ice (yes or no)	Dichotomous
Postweaning exercise variables (information obtained from owner at 3, 4, 6, and 12 mo of age)	
Daily use of stairs (yes or no)	Dichotomous
Daily walks on leash on asphalt or paved surface (yes or no)	Dichotomous
Daily walks on leash on gravel surface (yes or no)	Dichotomous
Daily walks on leash in forest, mountain, or other rough terrain (yes or no)	Dichotomous
Daily exercise in graveled run (yes or no)	Dichotomous
Daily exercise in run with soft (grass or dirt) surface (yes or no)	Dichotomous
Daily exercise in run with hard (concrete or asphalt) surface (yes or no)	Dichotomous
Daily exercise off leash in garden or yard (yes or no)	Dichotomous
Daily exercise off leash in park terrain (yes or no)	Dichotomous
Daily exercise off leash in forest, mountain, or other rough terrain (yes or no)	Dichotomous
Daily running alongside a moving bicycle (yes or no)	Dichotomous
Other daily exercise or activities (yes or no)	Dichotomous

For each dog, information was obtained from written questionnaires completed by the breeder and owner.