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Original Article**Genetic correlations of hip dysplasia scores for Golden retrievers and Labrador retrievers in France, Sweden and the UK**

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Highlights

- Hip dysplasia (HD) genetic parameters were estimated for two dog breeds in France, Sweden and the UK.
- Estimates of heritability ranged from 0.15 to 0.41, according to breed and country.
- The power of estimation was highly associated with the connectedness between populations.
- Genetic progress to reduce the prevalence of HD could be improved by selection across countries.
- Estimated genetic correlations of HD scores demonstrated the feasibility of international evaluation.

Abstract

In order to reduce the prevalence of inherited diseases in pedigree dogs, the feasibility of implementation of an international breeding program was investigated. One prerequisite is a strong genetic correlation between countries and our objective was to estimate this correlation for canine hip dysplasia (HD) across three countries to evaluate the feasibility of an international genetic evaluation. Data were provided by the Société Centrale Canine (SCC, France), Svenska Kennelklubben (SKK, Sweden) and The Kennel Club (KC, UK) on Golden retriever and Labrador retriever dogs. Trivariate analysis on the three different modes of scoring HD in France, Sweden and the UK was performed using a mixed linear animal model. Heritability, genetic correlation, number of common sires, genetic similarity, selection differentials and accuracy of selection were calculated.

The estimated heritabilities of Golden retrievers (Labrador retrievers) for HD scores were 0.28 (0.15), 0.28 (0.29) and 0.41 (0.34) in France, Sweden and the UK, respectively. The feasibility of performing a genetic evaluation of HD across countries was indicated by the favourable genetic correlations estimated between score modes (ranged from 0.48 to 0.99). The accuracy of selection for the most recent birth year cohorts of male dogs was not improved by international evaluation compared to national evaluation. Improvement in genetic progress can however be achieved by selection across populations in different countries, particularly for small populations, which were indicated by the large difference between selection differentials based on the national and international evaluations.

Keywords: Best linear unbiased prediction; Dog; Genetic correlation; Hip dysplasia; International breeding program

Introduction

Canine hip dysplasia (HD) has been reported in more than 183 dog breeds, with a prevalence varying from 0.0 to 71.8%¹. There is a strong association between the clinical diagnosis of hip status and veterinary care and mortality related to HD (Malm et al., 2008). Therefore, improving the hip status as measured during routine screening can benefit the health and welfare of pedigree dogs. Because multiple genes and environmental factors influence HD, selection based on breeding values is the best option to create a long-lasting and widespread improvement in health and welfare. Many studies have reported heritabilities of HD (0.01 – 0.75; Mäki et al., 2000; Dietschi et al., 2003; Malm et al., 2008; Lewis et al., 2010; Stock et al., 2011; Wilson et al., 2012; Oberbauer et al., 2017; Wijnrocx, 2017) and some have observed favourable genetic progress in reducing expression (Malm et al., 2008; Lewis et al., 2013; Oberbauer et al., 2017). However, genetic progress can be difficult to achieve for small populations where sufficient data to enable effective selection is lacking. Meanwhile, within a country, high selection intensity can increase the inbreeding level, which is a general risk factor for the expression of inherited diseases (Leroy and Baumung, 2011). Hence, enlarging the size of the population available for selection by combining data from several countries could be beneficial.

To achieve high accuracy for genetic evaluations across countries, the traits measured in each country must show strong genetic correlations. Investigators previous demonstrated feasibility of international genetic selection for HD by observing strong and favourable genetic correlations for HD between Sweden and the UK (Fikse et al., 2013). However, the genetic correlations in that study were estimated using correlations between nationally

¹ See: Orthopedic Foundation for Animals, 2016. http://www.ofa.org/stats_hip.html (Accessed 23 July 2017).

estimated breeding values. Therefore, we sought to estimate genetic correlations for HD between countries by combining pedigrees and phenotypic records from three countries (France, Sweden and the UK) for two breeds – Golden retrievers and Labrador retrievers – to investigate if genetic progress and accuracy of selection can be improved by selection across countries.

Materials and methods

The Société Centrale Canine (SCC, France), Svenska Kennelklubben (SKK, Sweden), and The Kennel Club (KC, UK) provided information on both pedigrees and phenotypic records of HD for two dog breeds: Golden retrievers and Labrador retrievers. For each breed, the pedigree databases from the three countries were merged into one combined pedigree database by identifying and replacing IDs for the individual dogs listed with more than one ID (Wang et al., 2017). After merging, the combined pedigree database contained 667,277 records for Golden Retrievers and 1,426,542 records for Labrador retrievers.

Three grading systems are widely used throughout the world: the FCI (Fédération Cynologique Internationale), the OFA (Orthopedic Foundation for Animals), and the BVA/KC (British Veterinary Association/The Kennel Club) modes. The scoring modes for HD are not the same in the three countries (Table 1). France follows the FCI system, which grades HD into five categories (A–E). For the diagnosis of HD in the FCI system, A and B are normal, C is mild, D is moderate and E is severe hip dysplasia. Sweden had a (different) five-level grading system for HD before 2000, and thereafter, Sweden started to follow the FCI system. The UK uses the BVA/KC system, which has nine features for each hip scored from 0-6, except one feature which is scored from 0-5. Summing up the scores from the nine

features for two legs, the total HD score (H) ranges from 0-106 in the UK (the lower the total score, the better the HD).

We regarded the score mode in each country as a separate trait to measure HD and transformed the scores to better follow a normal distribution. For French HD scores, the levels of HD (A, B, C, D, and E) were replaced with 1, 2, 3, 4, and 5, respectively. For Swedish HD scores, each grade of HD was first transformed to a normal score, and this was done separately for the two scoring systems. The normal scores were subsequently linearly transformed to get the desired values of 1 and 2 for dogs with A and B scores, respectively (Malm et al., 2008). For the UK HD score (UK), a natural log transformation was calculated as: $y_{UK} = \log_e(1 + H)$, where H is the total hip score adding the right and left hip scores together (Lewis et al., 2010). Phenotypic records were removed if there was a missing birth date of the individual, date of screening, clinic ID (specific to Sweden) or litter ID.

Calculations

A trivariate analysis of the HD records from the three countries was performed for each breed. This is later referred to as an international evaluation. Using the same model and the same data but assuming no genetic correlations between HD scores from the three countries is later referred to as a national evaluation. The analysis was run with mixed linear models using DMU software², and the genetic model was as below:

² See: Madsen, P., Jensen, J., 2013. A User's Guide to DMU.
http://dmu.agrsci.dk/DMU/Doc/Current/dmuv6_guide.5.2.pdf. (Accessed 23 July 2017)

$$\begin{bmatrix} \mathbf{y}_{FR} \\ \mathbf{y}_{SE} \\ \mathbf{y}_{UK} \end{bmatrix} = \begin{bmatrix} \mathbf{X}_{FR} & 0 & 0 \\ 0 & \mathbf{X}_{SE} & 0 \\ 0 & 0 & \mathbf{X}_{UK} \end{bmatrix} \begin{bmatrix} \mathbf{b}_{FR} \\ \mathbf{b}_{SE} \\ \mathbf{b}_{UK} \end{bmatrix} + \begin{bmatrix} \mathbf{Z}_{FR} & 0 & 0 \\ 0 & \mathbf{Z}_{SE} & 0 \\ 0 & 0 & \mathbf{Z}_{UK} \end{bmatrix} \begin{bmatrix} \mathbf{a}_{FR} \\ \mathbf{a}_{SE} \\ \mathbf{a}_{UK} \end{bmatrix} + \begin{bmatrix} \mathbf{W}_{FR} & 0 & 0 \\ 0 & \mathbf{W}_{SE} & 0 \\ 0 & 0 & \mathbf{W}_{UK} \end{bmatrix} \begin{bmatrix} \mathbf{l}_{FR} \\ \mathbf{l}_{SE} \\ \mathbf{l}_{UK} \end{bmatrix} \\ + \begin{bmatrix} 0 \\ \mathbf{U}_{SE} \\ 0 \end{bmatrix} \mathbf{c} \mathbf{y}_{SE} + \begin{bmatrix} \mathbf{e}_{FR} \\ \mathbf{e}_{SE} \\ \mathbf{e}_{UK} \end{bmatrix}$$

where \mathbf{y}_i is the vector of phenotypic values for country i . \mathbf{X} , \mathbf{Z} , \mathbf{W} and \mathbf{U} (\mathbf{b} , \mathbf{a} , \mathbf{l} and $\mathbf{c} \mathbf{y}$) are incidence matrices (solution vectors) for fixed effects, additive genetic effects, litter effects and clinic-year effects, respectively. The vector of fixed effects consisted of different factors for each trait: for France, it included sex, birth year and birth month; for Sweden, it included sex, birth month, year of examination, method of sedation, and a third-degree polynomial of age at screening; for UK, it included sex, birth year, birth month, age at screening and year of examination. The vector of additive genetic effects followed the multivariate normal distribution:

$$\begin{bmatrix} \mathbf{a}_{FR} \\ \mathbf{a}_{SE} \\ \mathbf{a}_{UK} \end{bmatrix} \sim N \left(\mathbf{0}, \begin{bmatrix} \mathbf{A} \sigma_{a_{FR}}^2 & \mathbf{A} \sigma_{a_{FR} a_{SE}} & \mathbf{A} \sigma_{a_{FR} a_{UK}} \\ \mathbf{A} \sigma_{a_{FR} a_{SE}} & \mathbf{A} \sigma_{a_{SE}}^2 & \mathbf{A} \sigma_{a_{SE} a_{UK}} \\ \mathbf{A} \sigma_{a_{FR} a_{UK}} & \mathbf{A} \sigma_{a_{SE} a_{UK}} & \mathbf{A} \sigma_{a_{UK}}^2 \end{bmatrix} \right);$$

where \mathbf{A} is the numerator relationship matrix using pedigree information trimmed for available HD records and σ_a^2 is the additive genetic variance; the vector of litter effects was assumed to follow a multivariate normal distribution without any covariances:

$$\begin{bmatrix} \mathbf{l}_{FR} \\ \mathbf{l}_{SE} \\ \mathbf{l}_{UK} \end{bmatrix} \sim N \left(\mathbf{0}, \begin{bmatrix} \mathbf{I} \sigma_{l_{FR}}^2 & 0 & 0 \\ 0 & \mathbf{I} \sigma_{l_{SE}}^2 & 0 \\ 0 & 0 & \mathbf{I} \sigma_{l_{UK}}^2 \end{bmatrix} \right);$$

the vector of clinic-year effects (SE only) followed a normal distribution:

$$\mathbf{cy}_{SE} \sim N(\mathbf{0}, \mathbf{I}\sigma_{cySE}^2);$$

and the residual vector was assumed to be multivariate normally distributed:

$$\begin{bmatrix} \mathbf{e}_{FR} \\ \mathbf{e}_{SE} \\ \mathbf{e}_{UK} \end{bmatrix} \sim N\left(\mathbf{0}, \begin{bmatrix} \mathbf{I}\sigma_{eFR}^2 & 0 & 0 \\ 0 & \mathbf{I}\sigma_{eSE}^2 & 0 \\ 0 & 0 & \mathbf{I}\sigma_{eUK}^2 \end{bmatrix}\right).$$

Genetic similarity (*GS*) between populations was calculated as the proportion of screened offspring of common sires (with screened offspring in two populations) in relation to the total number of screened offspring in the two populations (Rekaya et al., 1999):

$$GS_{ij} = \frac{\sum_{k=1}^{N_{ij}} (n_{ik} + n_{jk})}{\sum_{k=1}^{N_i} n_{ik} + \sum_{k=1}^{N_j} n_{jk}}$$

where N_{ij} is the number of sires with offspring in countries i and j , N_i and N_j are the number of sires in countries i and j , respectively, and n_{ik} and n_{jk} are the number of progenies of sire k in countries i and j , respectively.

Selection differentials (S) for male dogs born 2010-2014 were calculated for two scenarios: selection within country and selection across countries. In the first scenario, EBVs from national genetic evaluations were used to identify the 100 male dogs of highest genetic merit. EBVs from international genetic evaluation were used in the second scenario to identify the top 100 male dogs among all male dogs, irrespective of the country from which

they had information. EBVs used to rank male dogs and to calculate selection differentials were on transformed scales. Selection differentials were computed with the formula below (Mark et al. 2002):

$$S = \frac{(\bar{y}_{100} - \mu)}{\sigma_a}$$

where \bar{y}_{100} is the mean international EBV for the 100 top-ranking (national or international) male dogs born 2010-2014, μ is the mean international EBV of all male dogs born 2010-2014, and σ_a is the estimated genetic standard deviation (the square root of estimated additive genetic variance) based on the international evaluation. To make the two scenarios comparable, values from international evaluations were used for all three parameters mentioned above. The international EBVs were always expressed on the appropriate national scale, i.e., using \mathbf{a}_{FR} for French dogs.

For the calculation of the accuracy of selection (r), male dogs born 2010-2014 that received EBVs from both national and international evaluations were used. The accuracy of selection was calculated separately for the estimation of EBVs based on the national and international evaluation and was defined as:

$$r = \sqrt{1 - PEV/\sigma_a^2}$$

where PEV is the prediction error variance of EBV for each male dog (obtained from the sparse inverse of the mixed model equations) and σ_a^2 is the estimated additive genetic variance based on national (international) evaluations.

Results

Descriptive statistics

For Golden retrievers, Sweden had the largest number of phenotypic records (48,405), while for Labrador retrievers, the UK had the largest number of phenotypic records (79,341; Table 2). France had the lowest number of phenotypic records for both Golden retrievers and Labrador retrievers. In all three countries, average HD scores were higher (i.e., more unfavourable) for Golden retrievers than for Labrador retrievers. More details of the distribution of French, Swedish and the UK HD scores can be viewed in Table S1, Table S2 and Table S3. In addition, the proportion of individuals in the pedigree database with HD records can be viewed in Table S4 for each country.

Common sires and genetic similarity

For both breeds, Sweden and UK had the largest numbers of common sires (214 and 363, respectively), whereas France and Sweden had the smallest numbers of common sires (20 and 59, respectively; Table 4). Similar to the number of common sires, for both breeds, the genetic similarity between Sweden and UK was the largest, and the one between France and Sweden was the smallest. Furthermore, genetic similarities were higher for Labrador retrievers than for Golden retrievers.

Estimation of heritabilities and genetic correlations

For Golden retrievers, French scores and Swedish scores had equal heritabilities (0.28 and 0.28, respectively) which were lower than the heritability for the UK HD score (0.41; Table 3). For Labrador retrievers, the heritability for French scores (0.15) was much lower than heritabilities for Swedish scores (0.29) and UK (0.34). The heritabilities for Swedish

scores were similar between breeds. However, the heritabilities for French and UK scores were substantially different between Golden retrievers and Labrador retrievers.

The genetic correlations between French scores and UK scores were the lowest for both Golden retrievers (0.58) and Labrador retrievers (0.49; Table 4). The genetic correlation between French scores and Swedish scores (0.99) was the highest for Golden retrievers, and the genetic correlation between Swedish scores and UK scores (0.82) was the highest for Labrador retrievers (Table 4). For both Golden retrievers and Labrador retrievers, the standard errors of genetic correlations between French scores and Swedish scores (average 0.36) were the highest, and the ones between Swedish scores and UK scores (average 0.09) were the lowest.

Selection differentials and accuracy of selection

Based on national evaluation, for Golden retrievers, Sweden had the highest, and UK had the lowest absolute selection differentials; while for Labrador retrievers, UK had the highest, and France had the lowest absolute selection differentials (Table 5). Absolute selection differentials for both breeds resulting from the international evaluation were larger than those resulting from the national evaluation, with the exception of selection differentials of UK for Labrador retrievers, which were almost equal between the international and national evaluations. Furthermore, numbers of common top-100 ranking male dogs between the national and international evaluations were few for France for Golden retrievers (4) and Labrador retrievers (4) and for Sweden for Labrador retrievers (18), while other numbers of common top-100 ranking male dogs were much higher (52-100), which could explain the highest absolute selection differential.

Sweden had the highest accuracy of selection, while France had the lowest accuracy of selection for both breeds based on national evaluation (Table 6). International EBVs were slightly more reliable than national EBVs.

Discussion

By combining data from the three countries (including pedigrees and phenotypic records), we estimated the genetic correlations among the score modes of HD used in France, Sweden and the UK and investigated if the genetic progress and accuracy of selection of HD can be improved by genetic selection across counties.

The heritabilities of HD estimated in this study were within the range reported by previous studies (0.01 – 0.75; Mäki et al., 2000; Dietschi et al., 2003; Malm et al., 2008; Lewis et al., 2010; Stock et al., 2011; Wilson et al., 2012; Oberbauer et al., 2017; Wijnrocx, 2017). The heritabilities used for Golden retrievers and Labrador retrievers in the routine genetic evaluation carried out by SKK were 0.31 and 0.32 (S. Malm, personal communication), respectively, compared to 0.28 and 0.29 in the present study. Values of heritabilities of Swedish scores estimated in our study were slightly lower than those estimated by routine SKK, which is because the random effect of litter was not included in the Swedish HD evaluation routine but was in our genetic model. Lewis et al. (2010) reported heritabilities of 0.42 for Golden retrievers and 0.33 for Labrador retrievers in UK, which is similar to our results for UK (0.41 for Golden retrievers and 0.34 for Labrador retrievers). In Belgium, Wijnrocx (2017) estimated heritabilities of 0.26 for Golden retrievers and 0.13 for Labrador retrievers, while in USA, Oberbauer et al. (2017) estimated heritabilities of 0.65 for Golden retrievers and 0.59 for Labrador retrievers based on a specific HD score. Differences in heritability estimates can be explained by various factors (e.g., statistical model, type of HD

score, genetic background, sampling variation). In agreement with previous studies, our heritabilities were higher in Golden retrievers compared with Labrador retrievers in France and UK. Lewis et al. (2013) found quite consistent heritability value across breeds, stating that most of the observable variation in estimates was due to sampling variation. From a comparison between the different studies, it appears that the statistical model and type of HD score used impact the estimate of heritability.

In a previous study on gene flow between countries, we showed that a large part of founder contributions of French and Swedish Labrador retrievers was due to the UK founders (Wang et al., 2017), which implied a strong connection between Labrador retrievers populations in the UK and France and in the UK and Sweden. In the present study, the strong genetic connectedness of Labrador retrievers populations between the UK and Sweden was also reflected by the large number of common sires shared between the two countries ($n=363$; Table 4).

Genetic correlations estimated were favourable (ranged from 0.48 to 0.99) in our study, which confirmed the possibility of performing genetic evaluations of HD across countries. Fikse et al., (2013) reported that the absolute value of the genetic correlation between Sweden and the UK estimated for Labrador retrievers (1.03) was stronger than the one for Golden retrievers (0.87). In our study, the genetic correlation of Swedish scores and UK scores estimated for Labrador retrievers (0.82) was also stronger than the one for Golden retrievers (0.67). Comparing the genetic correlations estimated to the corresponding numbers of common sires and genetic similarity, higher genetic correlations were not fully related to higher numbers of common sires and genetic similarity. However, there is a strong inverse

relation between the number of common sires and the standard error of the genetic correlation between countries.

For the national evaluation, the largest populations tend to have the highest values of selection differentials (Table 5). The genetic improvement/progress in the larger populations in each breed was not obvious by across-country evaluation, particularly the absolute difference of selection differentials of UK scores for Labrador retrievers between the national and international evaluations were almost equal to zero. However, small populations can benefit from a much greater increase in genetic progress than larger populations by going from national to across-country selection, which was shown by the large absolute difference in selection differentials from the national and international evaluations of French scores for Golden retrievers and Labrador retrievers and of Swedish scores for Labrador retrievers.

Three factors influence the number of common male dogs in the 100 top-ranking between national and international evaluations: the average genetic level, the reliability of breeding values and the population size of the local population in comparison to the other populations. Top rankings are about identifying extremes in a population of selection candidates, and a higher average level, higher reliability and larger population size increase the probability of finding extreme individuals. In this study, the reliability was lowest for France and the French population was smallest in comparison with the other two countries, and are reasons why the numbers of common male dogs were the lowest in France for both Golden retrievers ($n=4$) and Labrador retrievers ($n=4$).

Moreover, the absolute difference of selection differentials between the national and international evaluations was inversely correlated to the number of common male dogs ranked

in the top-100 between the national and international evaluations. If the same 100 male dogs are also ranked at the top in the international evaluation, the selection differential should in reality be the same, which was shown in UK for Labrador retrievers. The same relationship between those two measures was found for genetic evaluation of udder health in dairy cattle (Mark et al., 2002).

Larger populations tended to have higher values for accuracy of selection based on national evaluations (Table 6). Apart from farm animals, improvement in accuracy of selection using international evaluation have been reported in dogs (Arvelius et al., 2013) and horses (Viklund et al., 2015). In our study, the accuracy of selections for male dogs born 2010-2014 were similar between national and international evaluations, which could be because the extra information from international genetic information is mainly contributes to the parents of these dogs. Most of the common sires (Table 4) were born before 2010, and for those, reliability of international EBV is expected to benefit more due to HD records of offspring in multiple countries. Therefore, reliability of international EBV for the male dogs born 2010-2014 is expected to benefit more in the future, because more HD records of offspring in multiple countries will be collected.

Dog breeding is an international activity and international collaboration was called for to promote the improvement of genetic health in pedigree dogs (Hedhammar et al., 2011). Referring to the model of International Bull Evaluation Service (INTERBULL), initialization of an international genetic evaluation platform for inherited disorders in the dog was proposed (Woolliam et al., 2011; Wilson and Wade, 2012). Currently, national genetic evaluation systems for HD have been implemented in some countries (Denmark, Finland, Germany, Norway, Sweden and the UK) for a number of breeds and in some other countries it is under

development (e.g., France). Beyond the potential political and financial issues that need to be discussed, such a collaboration might be easier to start between countries that already have national evaluation systems.

In this study, we focused on estimating the genetic correlation of HD scores across countries, which can be helpful for the development of operational tools to improve the HD in an international context. That the type of HD scoring varies across countries is a potential weakness for the implementation of international evaluation of HD and it may impact genetic correlations between countries. Nevertheless, high reliability of international evaluations between Sweden and the UK was shown by high genetic correlations (average 0.75) and low standard errors (average 0.09). A high genetic correlation can be considered as one of the prerequisites, in addition to, e.g., financial resources to initialize an international evaluation platform, agreement on day-to-day exchanging of data, EBV computation routine and reporting system, to start an international evaluation for HD (Wilson and Wade, 2012).

Simulation studies carried out by varying genetic correlation showed that breeding programs could benefit from mutually selecting sires and dams from each other when the genetic correlation was as low as 0.4 to 0.6 in the initial generations of selection (Mulder and Bijma, 2006), however, the genetic correlation as high as 0.8 to 0.9 was required to achieve significant improvement of genetic gain. Therefore, we highly recommend kennel clubs to promote the HD screening of dogs with at least one of the parents originating from a foreign country, because this can increase the connectedness between countries and consequently increase the power of genetic correlation estimation. Because dog breeding is characterized by various breeding practices and regulations across countries (Shariflou et al. 2011, Hedhammar

et al. 2011), methods to promote the HD screening should be further discussed case by case in each country.

Until now, no published paper has reported the analysis of genetic parameters of HD score in the French dog population. Our study is the first one to estimate variance components and heritabilities of HD for French breeds using a mixed linear animal. Under univariate analysis, the accuracies of selection for HD in French populations for both breeds (average 0.39) were lower than the accuracies of selection for HD in the Swedish and UK populations (average 0.65). Compared to the data provided by Sweden and the UK, insufficient phenotypic information may be the reason for the low accuracy in the French populations, for instance, poor HD scores (D and E) may be preferentially not submitted (Table S1) and some fixed effects related information, e.g., test date, is lacking. Furthermore, compared to the number of dogs registered in the pedigree databases, the proportions of individuals with HD records were low for both Golden retrievers and Labrador retrievers in France (Table S4). Therefore, to implement a genetic evaluation of HD in France and obtain higher reliabilities, a larger number of HD records should be obtained; awareness should be raised to encourage breeders and owners to screen their dogs.

It has been suggested that because HD score is a categorical trait, a threshold model (TM) would be superior to a linear model (LM) (Silvestre et al, 2007). They found very little difference between TM and LM regarding, e.g., genetic parameters and genetic trends, but a rather low rank correlation between EBVs from the two models (0.73). This would indicate substantial re-ranking among the potential candidates. However, they did point out that the low rank correlations they found are in contrast to other studies comparing TM and LM. Their study was also based on only around 300 dogs with phenotypes and they had a less

complicated model, with no clinic-year or litter effects. One problem with TM is the so-called extreme category problem, which creates estimability problems when, e.g., all individuals in a litter have the same score (e.g. A). Therefore, even though TMs are theoretically more correct, they have often been rejected in favour of LM, which is more robust for practical purposes.

In this study, we estimated the genetic correlations between the FCI and BVA/KC score modes of HD; future research could also take the OFA mode into consideration. Future research could also focus on investigating breeding strategies to assist the determination of breeding guidance and policy for kennel organizations on genetic management of HD at an international scale. For example, enlarging the pool of selection candidates by means of international genetic evaluations could be used not only to enhance genetic progress (illustrated here by selection differentials) but also to manage inbreeding. Moreover, knowledge regarding the effect of factors such as the proportion of dogs with HD score, or the connectedness between subpopulations across countries (e.g., number of common sires, number of average offspring recorded in each country) on the reliability of international EBVs, through simulation for instance, should also be useful for kennel clubs as benchmarking criteria to prepare sufficient data to initialize or join an international evaluation.

Conclusions

The possibility of performing genetic evaluations of HD across countries was confirmed by the favourable genetic correlations estimated in our study between different score modes of HD in France, Sweden and the UK. The existence of connections between populations, also an important prerequisite for international evaluations, was illustrated by the numbers of common sires shared between countries. Enlarging the population size of

selection candidates through combining data from different countries can increase the genetic progress of HD, particularly for small populations. The accuracy of selection for the most recent birth year cohorts of male dogs was only marginally improved by international evaluation compared to national evaluation.

Conflict of interest statement

None of the authors has any financial or personal relationships that could inappropriately influence or bias the content of the paper.

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References

- Arvelius, P., Klemetsdal, G., 2013. How Swedish breeders can substantially increase the genetic gain for the English Setter's hunting traits. *Journal of Animal Breeding and Genetics* 130, 142-153.
- Dietschi, E., Schawalder, P., Gaillard, C., 2003. Estimation of genetic parameters for canine hip dysplasia in the Swiss Newfoundland population. *Journal of Animal Breeding and Genetics* 120, 150-161.
- Fikse, W.F., Malm, S., Lewis, T.W., 2013. Opportunities for international collaboration in dog breeding from the sharing of pedigree and health data. *The Veterinary Journal* 197, 873-875.
- Hedhammar, Å.A., Malm, S., Bonnett, B., 2011. International and collaborative strategies to enhance genetic health in purebred dogs. *The Veterinary Journal* 189, 189-196.
- Leroy, G., Baumung, R., 2011. Mating practices and the dissemination of genetic disorders in domestic animals, based on the example of dog breeding. *Animal Genetics* 42, 66-74.
- Lewis, T.W., Blott, S.C., Woolliams, J.A., 2010. Genetic evaluation of hip score in UK Labrador Retrievers. *PLoS ONE* 5, e12797.
- Lewis, T.W., Blott, S.C., Woolliams, J. A., 2013. Comparative analyses of genetic trends and prospects for selection against hip and elbow dysplasia in 15 UK dog breeds. *BMC Genetics* 14, 1.
- Madsen, P., Jensen, J., 2013. A User's Guide to DMU.
http://dmu.agrsci.dk/DMU/Doc/Current/dmuv6_guide.5.2.pdf.
- Malm, S., Fikse, W.F., Danell, B., Strandberg, E., 2008. Genetic variation and genetic trends in hip and elbow dysplasia in Swedish Rottweiler and Bernese Mountain Dog. *Journal of Animal Breeding and Genetics* 125, 403-412.
- Malm, S., Fikse, F., Egenvall, A., Bonnett, B. N., Gunnarsson, L., Hedhammar, Å., 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. *Preventive Veterinary Medicine* 93, 222-232.
- Mark, T., Fikse, W.F., Emanuelson, U., Philipsson, J., 2002. International genetic evaluations of Holstein sires for milk somatic cell and clinical mastitis. *Journal of Dairy Science* 85, 2384-2392.
- Mäki, K., Liinamo, A. E., Ojala, M., 2000. Estimates of genetic parameters for hip and elbow dysplasia in Finnish Rottweilers. *Journal of Animal Science* 78, 1141-1148.
- Oberbauer, A. M., Keller, G. G., Famula, T. R. 2017. Long-term genetic selection reduced prevalence of hip and elbow dysplasia in 60 dog breeds. *PloS one*, 12, e0172918.

- Rekaya, R., Weigel, K., Gianola, D., 1999. Estimation of parameters of structural model for genetic covariances in international genetic evaluations. *Interbull Bulletin* 22, 25.
- Shariflou, M. R., James, J. W., Nicholas, F. W., Wade, C. M. 2011. A genealogical survey of Australian registered dog breeds. *The Veterinary Journal* 189, 203-210.
- Silvestre, A. M., Ginja, M. M. D., Ferreira, A. J. A., Colaco, J. 2007. Comparison of estimates of hip dysplasia genetic parameters in Estrela Mountain Dog using linear and threshold models. *Journal of animal science* 85, 1880-1884.
- Stock, K.F., Klein, S., Tellhelm, B., Distl, O., 2011. Genetic analyses of elbow and hip dysplasia in the German shepherd dog. *Journal of Animal Breeding and Genetics* 128, 219-229.
- Viklund, Å., Furre, S., Eriksson, S., Vangen, O., Philipsson, J., 2015. Genetic conditions of joint Nordic genetic evaluations of lifetime competition performance in warmblood sport horses. *Journal of Animal Breeding Genetics* 132, 308-317.
- Wang, S., Leroy, G., Malm, S., Lewis, T., Strandberg, E., Fikse, W.F., 2017. Merging pedigree databases to describe and compare mating practices and gene flow between pedigree dogs in France, Sweden and the UK. *Journal of Animal Breeding and Genetics* 134, 152-161.
- Wijnrocx, K., 2017. Sustainable breeding of pedigree dogs. PhD thesis. KU Leuven, Belgium.
- Wilson, B.J., Wade, C.M., 2012. Empowering international canine inherited disorder management. *Mammalian Genome* 23, 195-202.
- Wilson, B.J., Nicholas, F.W., James, J.W., Wade, C.M., Tammen, I., Raadsma, H. W., Thomson, P. C., 2012. Heritability and phenotypic variation of canine hip dysplasia radiographic traits in a cohort of Australian German shepherd dogs. *PLoS ONE* 7, e39620.

Table 1

Hip dysplasia (HD) scores before and after data transformation in France, Sweden and the UK

Country	HD scores	After transformation
France	A, B, C, D, E	1, 2, 3, 4, 5
Sweden	Normal, Grade I, Grade II, Grade II, Grade IV (Until 1999)	1.3, 2.6, 3.1, 3.6, 4.5
	A, B, C, D, E (Since 2000)	1.0, 2.0, 2.5, 3.0, 3.7
UK	0 - 106 for each dog (0 – 53 for each leg)	0 - 4.67

Table 2

Summary of description statistics of hip dysplasia (HD) scores for Golden retrievers and Labrador retrievers

Breed	Trait	<i>n</i>	Average	S.D.	Min value	Max value
	FR	5,798	1.65	0.82	1.00	5.00
GDR	SE	48,405	1.67	0.71	1.00	4.50
	UK	27,023	2.66	0.60	0.00	4.67
	FR	7,080	1.53	0.75	1.00	5.00
LBR	SE	41,073	1.54	0.68	1.00	4.50
	UK	79,341	2.41	0.65	0.00	4.67

SD, Standard deviation; Min, Minimum; Max, Maximum; FR, French HD score, SE, Swedish HD score; UK, UK HD Score; GDR, Golden retrievers; LBR, Labrador retrievers

Table 3

Estimated variance components and heritabilities (standard error) of hip dysplasia (HD) scores for Golden retrievers and Labrador retriever (LDR) from the trivariate model

Breed	Trait	Animal	Clinics	Litter	Residual	Total	Heritability ^a
GDR	FR	0.18	-	0.05	0.42	0.65	0.28
		(0.02)		(0.01)	(0.02)	(0.05)	(0.03)
	SE	0.15	0.01	0.02	0.34	0.52	0.28
		(0.01)	(0.00)	(0.00)	(0.00)	(0.02)	(0.01)
UK	UK	0.12	-	0.01	0.17	0.30	0.41
		(0.01)		(0.00)	(0.00)	(0.01)	(0.01)
LBR	FR	0.08	-	0.02	0.44	0.54	0.15
		(0.01)		(0.01)	(0.02)	(0.04)	(0.02)
	SE	0.14	0.01	0.04	0.29	0.47	0.29
		(0.01)	(0.00)	(0.00)	(0.00)	(0.02)	(0.01)
UK	UK	0.14	-	0.03	0.23	0.40	0.34
		(0.00)		(0.00)	(0.00)	(0.01)	(0.01)

FR, French HD score, SE, Swedish HD score; UK, UK HD Score; GDR, Golden retrievers; LBR, Labrador retrievers

$$^a \text{Heritability} = \frac{\text{Estimated additive genetic variance}}{\text{Sum of all variance components}}$$

Table 4

Estimated genetic correlations (standard error), number of common sires and average number of offspring with hip dysplasia (HD) records, and genetic similarity between HD scores in different countries for Golden retrievers and Labrador retrievers

Breed	Trait	Genetic correlation	Common sire			Genetic similarity	
			<i>n</i>	Average No. of recorded offspring			
				FR	SE		UK
GDR	FR–SE	0.99 (0.28)	20	1.60	4.60	-	0.002
	FR–UK	0.58 (0.22)	40	1.20	-	4.18	0.007
	SE–UK	0.67 (0.11)	21 4	-	1.88	3.94	0.02
LBR	FR–SE	0.50 (0.44)	59	4.41	8.93	-	0.02
	FR–UK	0.49 (0.27)	94	3.30	-	49.01	0.04
	SE–UK	0.82 (0.07)	36 3	-	8.31	48.17	0.24

FR, French HD score, SE, Swedish HD score; UK, UK HD Score; GDR, Golden retrievers; LBR, Labrador retrievers

Table 5

Comparison of selection differentials of hip dysplasia (HD) score between national (NAT) and international evaluations (INT) for sires born in 2010 – 14 for Golden retrievers and Labrador retrievers

Breed	Trait	Number of male dogs		Selection differentials			
		NAT	INT	NAT	INT	Δ	CMD
	FR	925	3,843	-0.88	-1.42	-0.54	4
GDR	SE	1,801	3,843	-1.03	-1.06	-0.02	90
	UK	1,132	3,843	-0.84	-0.95	-0.12	52
	FR	1,027	8,542	-0.66	-1.15	-0.49	4
LBR	SE	2,483	8,542	-0.99	-1.33	-0.34	18
	UK	5,109	8,542	-2.04	-2.04	0.00	100

FR, French HD score, SE, Swedish HD score; UK, UK HD Score; GDR, Golden retrievers; LBR, Labrador retrievers; CMD, number of common male dogs in 100 top-ranking between national and international evaluation

Table 6

Comparison of accuracy of selection of hip dysplasia (HD) score between national (NAT) and international evaluations (INT) for sires born in 2010 – 14 for Golden retriever and Labrador retrievers

Breed	Trait	Number of male dogs	Accuracy of selection	
			NAT	INT
	FR	925	0.49	0.50
GDR	SE	1,801	0.67	0.67
	UK	1,132	0.63	0.64
	FR	1,027	0.35	0.35
LBR	SE	2,483	0.66	0.67
	UK	5,109	0.62	0.63

FR, French HD score, SE, Swedish HD score; UK, UK HD Score; GDR, Golden retrievers; LBR, Labrador retrievers