



## Information regarding pedigree-based versus DNA-based inbreeding estimates

Information from the Scientific Committee of the Nordic Kennel Union, NKU/VK, regarding pedigree-based versus DNA-based inbreeding estimates.

Inbreeding in dogs refers to the mating of individuals that are related, which will lead to an increase in homozygosity, i.e., that an individual inherits two identical copies of a gene, one from each parent. Inbreeding and genetic variation are two sides of the same coin. Across species, it is known that high levels of inbreeding are associated with reduced fertility and increased risk of inherited disease. In addition, genetic variation is crucial for selection and genetic progress. One can estimate the degree of inbreeding for an individual, or the average level of inbreeding (or degree of genetic variation) in a population, for example within a breed. The level of inbreeding can be estimated using pedigree information or by DNA analysis, the latter often referred to as genomic inbreeding.

### Pedigree-based inbreeding

Pedigree-based inbreeding estimates are calculated using the known ancestry of a dog. The inbreeding coefficient is calculated based on the likelihood that two alleles at a given locus are identical because they are both inherited from a common ancestor. A pedigree based inbreeding estimate will only capture the inbreeding that has occurred in the generations included in the calculation, typically a few generations back.

For example, an inbreeding calculation based on a five-generation pedigree reflects the increase in inbreeding that has happened in the last five generations, and will not account for inbreeding that occurred in prior generations. It will therefore, most likely, be much lower than the level of inbreeding that has accumulated since the establishment of the breed.

Pedigree-based calculations of inbreeding can, nevertheless, be very useful in practical breeding. Regardless of the level of genetic variation in a breed (which is a result of the breeding that has been done in the past), it is important to avoid a rapid increase of inbreeding, to limit further loss of genetic variation. Moreover, “new inbreeding” and rapidly increasing inbreeding is often more harmful than historical, gradually accumulating inbreeding.

***Hence, pedigree-based estimates of inbreeding, going 5-6 generations back, are useful for the purpose of breeding planning, with respect to specific combinations. Regardless of the level of genetic variation in the breed or in an individual, the risk of disease and inbreeding depression in a specific litter will increase if the parents are closely related. Avoiding these high-risk combinations will also help to limit the rate of increased inbreeding in the population.***

However, to estimate the accumulated, total level of inbreeding in a breed, one must either use complete pedigrees, or DNA-based methods. Since the former can be difficult in practice due to lack of data, DNA analyses are often the best option.



## DNA-based estimates of inbreeding

In DNA-based analyses of genetic variation and inbreeding (genomic inbreeding), the dogs' DNA is examined directly. Genomic inbreeding is estimated by examining whether the dog is homozygous, i.e., lack genetic variation, in a larger proportion of their genes compared to other dogs. This can be done by examining the extent and length of runs of homozygosity (ROH), i.e., identical segments in an individual's genome due to inbreeding or selection for particular genes, or by comparing the number of individual markers that are homozygote in an individual dog to the number that would be expected in a dog that's not inbred.

The methods used for calculation of genomic inbreeding may vary between different commercial providers. Hence, the same individual may get diverse results from different companies. Consequently, results for dogs tested by different test providers are not directly comparable. In addition, the selection of dogs included in the analysis will influence the breed averages presented. Despite this, figures of DNA-based inbreeding found in different studies or with different commercial providers are often correlated. In other words, a breed that comes out well in one analysis will often come out quite well in another as well, and vice versa.

## How to interpret and implement DNA-based inbreeding estimates

Implementation of genomic inbreeding in breeding planning is not straightforward. On a population level, average genomic inbreeding will give an indication of the risk of inbreeding depression and the need to take action for preservation and/or addition of genetic diversity in the breed. However, there is currently not sufficient scientific basis to define a limit of an acceptable level for a DNA-based inbreeding estimate in a breed. Firstly, there are only a handful of publications on DNA-based inbreeding estimates in dogs and correlation with health parameters. Furthermore, the tolerance limit will likely not be the same for all breeds but will depend on, among other things, the current and historical breeding structure (e.g., historical versus new inbreeding), as well as the general health status of the breed and need to change/improve the breed by selection (need for rapid progress implies a greater need for genetic variation).

***For individual dogs, breeding recommendations related to genomic inbreeding are still lacking and are difficult to develop due to the lack of standardisation regarding definition and calculation.***

Hence, when comparing genomic inbreeding estimates from individual dogs, one should make sure that the results to be compared are from the same test provider. In addition, it's important to note that an individual dog's estimated genomic inbreeding coefficient is not a useful tool to assess the dog's suitability as a breeding animal, because even an inbred dog can have offspring that are not inbred if it is mated with an unrelated partner.

Matchmaking tools, allowing calculations of expected genomic inbreeding for offspring from a planned mating, are offered by some companies. These tools may provide useful information when choosing a stud dog, to monitor and limit the level of inbreeding in the offspring. However, the NKU Scientific Committee believes that DNA-based inbreeding tools are currently useful primarily to monitor and compare breeds at the *population level*. When planning individual breeding



combinations within a population, a pedigree-based inbreeding estimate will provide the information needed to avoid the highest risk combinations with respect to inbreeding.

***To conclude, a DNA-based estimate of genetic variation/level of inbreeding may be a useful tool, primarily at a population level, to assess the degree of genetic variation in the breed. Higher levels of inbreeding are associated with increased risk, but there is currently not sufficient evidence to define “how much is too much”. However, based on the precautionary principle, actions to increase diversity should be seriously considered in breeds where the levels of inbreeding are high.***