Longevity and major causes of death are heritable in Irish Wolfhound

C.J.A. van Gemert[1,2], J.J. Windig[2] and P. Berg[1,*]

[1] Norwegian University of Life Sciences, P.O. Box 5003, N-1432 Ås, Norway; [2] Wageningen University & Research, P.O. Box 338, 6700 AH Wageningen, the Netherlands; *Peer.Berg@nmbu.no

Abstract
Irish Wolfhound (IW) is a large dog breed developed several centuries ago with an average longevity of 7 years The genetics behind the short lifespan is poorly understood. Based on data from the Irish Wolfhound database (IWDB) on 118095 pedigreed IW and data from the IW Longevity Study including 10122 dogs with known longevity and 6057 of these having a known cause of death (COD), longevity and the two most common COD were analysed. Heritability, maternal effects, and correlations were estimated accounting for sex, birthyear, country of origin and inbreeding coefficient. Both longevity (0.27) and COD (0.17-0.20) were moderately heritable. Longevity and COD showed low correlations, both genetic and residual correlations. We argue that this is likely due to short longevity being caused by early aging and COD being specific expressions of early aging. In addition, inbreeding was found to significantly reduce longevity. Implications for increasing longevity in IW are discussed.

Introduction
Dogs are popular pet animals, displaying a large variation in size, color, temperament and behaviors. Dogs are the species with the most recorded genetic defects (OMIA 2022), which is also reflected in differences in health and longevity of different breeds. Larger breeds tend to have a shorter lifespan than smaller breeds because larger breeds tend to age more quickly (Kraus et al, 2013). Larger breeds spend relatively more energy to reach adult size than small breeds. Thereby they would have relatively less energy left for health maintenance (Fan et al, 2016). Giant and large breed dogs are also at an increased risk of osteosarcoma (bone cancer), relative to smaller breeds (Breur et al, 2001). So size has an important influence on longevity and disease risk in dog breeds.
The Irish wolfhound is a rough-coated dog known as the largest and tallest of all coursing breeds, though not the heaviest breed. Their minimum size is defined by the American Kennel Club as 81 cm for mature males and 76 cm for mature females. They are also characterized by a median longevity lower than expected. Leading causes of death for Irish Wolfhounds are dilated cardiomyopathy and bone cancer (Urfer et al, 2007), which are also the most reported causes of death for dog breeds in general, besides age (Lewis et al, 2018).
The objective of this paper is to evaluate the potential for selecting for a longer and healthier life for the Irish Wolfhound breed, by estimating genetic variation in longevity, main causes of death and their correlation.

Materials & Methods
Material. Data were obtained from the Irish wolfhound database (IWDB 2021), including an estimated 98% of all Irish wolfhounds ever registered. We used the complete and public IWDB dataset and the private Irish Wolfhound Longevity Study dataset. The pedigree used consists of 167132 dogs, from 1859 to 2020, with 11558 dogs having longevity records and 6057 of these having a recorded cause of death.
There are two possible causes of bias in the longevity records. First, the older animals have a potential recording bias since recording started in 2012, and recordings back in time are likely

to favor surviving and important older dogs. Secondly, animals born in recent years do not all have longevity records yet. This is illustrated in Figure 1, with a reduced longevity in recent years, solely due to incomplete recordings. We evaluated these causes of bias by analysing different subsets of data, including years 1859-2011, 1979-2013 and 1979-2020 respectively. Results of these analyses are not included here. Further analyses presented here are based on the 1979-2013 cohort, containing 118095 dogs in total, of which 10122 have longevity records and 6067 a known cause of death. There are 133 different classifications for cause of death (COD) recorded. Here we include the two most frequent categories, summarizing heart disease and cancer, recorded as 0/1. Data is summarized in Table 1.

Statistical analysis. For genetic analyses the following model was used:

$Y_{ijklm} = Sex_i + Country_j + BY_k + \beta \cdot F_i + a_l + c_m + e_{ijklm}$

Where Y is longevity or COD, Sex is male or female, Country is one of 18 countries of birth, BY is birth year, F is individual inbreeding coefficient calculated from pedigree, and a is random additive genetic effect, c is random common environmental dam effect and e is the residual.

Data were analysed using R 4.0.3 (R Core Team, 2020) and ASReml 4.1 (Gilmour et al, 2015) with uni- or bi-variate models. In bivariate models the common environmental dam effect c was excluded.

Results

Irish Wolfhound is characterised by a short average lifespan of 7.25 years, see Table 1. More than half of the dogs dies from one of the two most common categories heart disease and cancer. Average lifespan is slightly shorter in dogs categorized as having died from heart disease or cancer, with an average of 6.74 and 6.86 years respectively. Longevity is however highly variable with observations ranging from 0 to 5479 days (15 years). More specifically 18% were 5 years or younger, 57.7% were 7 years or older and 27.6% were 9 years or older. Figure 1 shows average longevity by birth year and a slight negative trend in longevity can be observed.

Table 1. Number of dogs with observations on longevity, cause of death (COD), prevalence of COD and mean longevity (days ± SD) of all dogs and those diagnosed with a specific COD.

Trait	N Obs	Prevalence	Mean longevity
Longevity	10114		2648 ± 925
COD Heart disease	6057	18%	2459 ± 804
COD Cancer	6057	34%	2503 ± 709

Heritability of longevity was estimated at 0.27 (Table 2), slightly higher than for the two main causes of death with heritabilities of 0.17 and 0.20, respectively. Thus, there is a large genetic variance in longevity, a genetic standard deviation of 482 days. Common environmental dam effects were small. Common environmental dam effects were left out of the model in bivariate analyses due to convergence problems.

The genetic correlation between cancer and longevity was positive but unfavorable, with increasing cancer resulting in increased longevity however the genetic correlation was not significantly different from zero. In contrast the genetic correlation between heart disease and longevity was favorable (-0.24) and significantly different from zero. Residual correlations between longevity and causes of death were low but unfavorable.

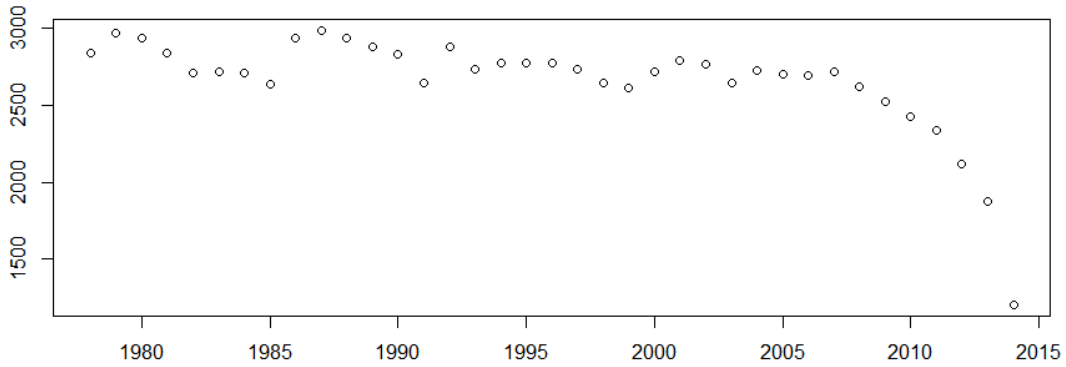

Figure 1. Mean longevity versus year of birth for Irish Wolfhound.

Inbreeding significantly affected longevity. An increase of the inbreeding coefficient of 1% unit (0.01 increase) decreased longevity by 9.6 (± 2.6) days, equivalent to a 0.4% reduction in longevity. Inbreeding did not significantly affect the two COD categories.

Table 2. Heritability, common litter effects, genetic (above diagonal) and residual (below diagonal) correlations (± SE).

Trait	h^2	c^2	Correlations		
			Longevity	COD heart	COD cancer
Longevity	0.27 ± 0.03	0.04 ± 0.01		-0.24 ± 0.09	0.10 ± 0.09
COD heart	0.17 ± 0.03	0.02 ± 0.02	0.06 ± 0.02		-[1]
COD cancer	0.20 ± 0.03	0.02 ± 0.02	0.01 ± 0.02	-[1]	

1. Not estimated.

Discussion

Longevity observed in this material is in agreement with longevity observed in previous studies on Irish Wolfhound (Simpson, 2016; Urfer et al. 2007).

We found a significant heritability and a large genetic standard deviation of longevity of 482 days. This indicates a large potential for increasing longevity by selection. However, there are at least two challenges. First, the current relatively low longevity is likely caused by previous selection for breed characteristics and/or the severe bottlenecks that the breed has experienced during its history. Size is an important breed characteristic, but generally size is known to be negatively related to longevity across breeds and the main effect seems to be an earlier onset of aging (Kraus et al. 2013). Thus, a better understanding of the relationship between breed standard and health/longevity is needed. Secondly, both longevity and cause of death are observed late in life, most often after reproductive life. Thus, selection of young individuals can only be done with low accuracy, unless genetic evaluation utilizing information from relatives are implemented. Even more promising would be the implementation of genomic selection which would allow for increased accuracy on young dogs (Meuwissen et al. 2001). Jointly, these two challenges point to the need for early indicators of health and longevity. Promising indicators could likely be related to early indicators of aging.

Genetic and residual correlations between longevity and the two main causes of death were low and generally close to zero. This can be explained by the specific causes of death being a consequence of faster aging, but that the specific cause of death is partly caused by other loci in addition to environmental effects. A specific and common heart disease, dilated

cardiomyopathy, has been found to be affected by three loci on chromosomes 1, 21, and 37 of Irish Wolfhound (Simpson et al, 2016; Philipp et al, 2012).
We found a significant and unfavorable effect of inbreeding on the longevity of an individual. This implies that there are deleterious recessive alleles for longevity segregating in the population. Targeting these specific loci would require a large genotyping effort and would take a long time since samples for genotyping of ancestral individuals does not exist. Alternatively, the effect of inbreeding can be counteracted by the use of dogs from other breeds. However, this requires a continued gene flow from one or several other breeds to have a lasting effect on genetic diversity (Windig & Doekes, 2018).
In conclusion, our results document a large potential for genetically increasing health and longevity in Irish Wolfhound. In the short term the most promising route seems to be identification of early indicators of aging, and in the longer term the development of a genotyped and phenotyped reference population to allow accurate genetic evaluation of younger dogs.

References

Breur G. J., Lust G., & Todhunter R. J. (2001). Genetics of canine hip dysplasia and other orthopaedic traits. In: *The Genetics of the Dog. Ruvinsky A and Sampson J, ed CABI Publ, Wallingford, UK*, pp 267-98.
Fan R., Olbricht G., Baker X., & Hou C. (2016). *Aging (Albany NY)*, *8*(12), 3209. https://doi.org/10.18632/aging.101081
Gilmour, A. R., Gogel, B. J., Cullis, B. R., Welham, S. J. and Thompson, R. (2015). ASReml User Guide Release 4.1 Functional Specification. https://www.vsni.co.uk
IWDB (2021). https://iwdb.org/
Kraus C., Pavard S., & Promislow D. E. (2013). *The American Naturalist*, *181*(4), 492-505. https://doi.org/10.1086/669665
Lewis T. W., Wiles B. M., Llewellyn-Zaidi A. M., Evans K. M., & O'Neill D. G. (2018). *Canine genetics and epidemiology*, *5*(1), 1-17. https://doi.org/10.1186/s40575-018-0066-8
Meuwissen T.H.E., Hayes B.J., and Goddard M.E. (2001) Genetics 157(4):1819-1829. https://doi.org/10.1093/genetics/157.4.1819
OMIA, Online Mendelian Inheritance in Animals. Available at: https://www.omia.org/.
Philipp U., Vollmar A., Häggström J., Thomas A., & Distl O. (2012). *PLoS One*, *7*(6), e36691. https://dx.doi.org/10.1371%2Fjournal.pone.0036691
R Core Team (2020). https://www.R-project.org/.
Simpson S., Dunning M. D., Brownlie S., Patel J., Godden M., et al. (2016). *BioMed research international*, *2016*. https://doi.org/10.1155/2016/6374082
Urfer S. R., Gaillard C., & Steiger A. (2007). *Veterinary quarterly*, *29*(3), 102-111. https://doi.org/10.1080/01652176.2007.9695233
Windig J. J., & Doekes H. P. (2018). *Journal of Animal Breeding and Genetics*, *135*(3), 238-248. https://doi.org/10.1111/jbg.12330