759. Inbreeding and litter size in Dutch pedigreed dogs

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Abstract
Inbreeding may negatively affect fertility, especially when mating closely related individuals. We evaluated the frequency of these matings in Dutch pedigreed dogs between 1997 to 2018 and their effect on litter size in 15 breeds. The percentage of matings between half-cousins and closer has decreased since 1999. Litter size of individual matings tended to be significantly lower only for full sib and parent offspring matings. Inbreeding depression was only evident when analysed at the population level. In two breeds, a 1% increase in inbreeding of the dam resulted in an estimated reduction of litter size of 0.05 and 0.028 pups. These findings emphasize the importance for breeders and owners to avoid mating closely related dogs.

Introduction
Inbreeding is the result of mating related animals. Inbreeding can lead to the expression of genetic defects and inbreeding depression resulting in, e.g. a lower fertility (Falconer and Mackay 1996; Doekes *et al.* 2021). In many pedigreed dog breeds, inbreeding rates have been >0.5% per generation (Lewis *et al.*, 2015). To counteract the increase in inbreeding, mating between close relatives such as parent – offspring mating has been banned in breeds and kennel clubs. This does, however, not prevent inbreeding. Since pedigreed dogs form (small) closed populations high inbreeding rates may still occur and lead to inbreeding depression.

The effects of inbreeding may be (partly) compensated by natural and artificial selection. The heritability of fertility traits in dog populations tends to be low to moderate, i.e. in the range of 0.05 to 0.30 (Hare and Leighton, 2005; Leroy *et al.*, 2015). A decrease in fertility due to an increase in inbreeding may not be observed due to simultaneous selection for better fertility. Only when inbreeding rates are high, genetic drift is the main driver of allele frequency changes and selection cannot counteract the decrease in fertility over time due to inbreeding.

Pedigreed dogs provide an opportunity to investigate the effect of inbreeding on fertility. Litter sizes and relationships can be readily determined from pedigrees. Here, we used national pedigree data from the Dutch Kennel club to: (1) evaluate the frequency of close relative matings in the Netherlands from 1999 to 2018; (2) study the effect of these matings on litter size in 15 breeds; and (3) determine the amount of inbreeding depression in two of the breeds while accounting for a detailed pedigree.

Materials & methods
Data and classification of close relative matings. A data base was provided by the Dutch Kennel club. This data-base contained breed, birth date and father and mother of all registered pups of pedigreed dogs born in the Netherlands between 1997 and 2018. The following close relative matings were determined, with in brackets the corresponding relationship coefficients: parent – offspring (0.5), full sibs (0.5), half sibs (0.25), grandparent – grandchild (0.25), full uncle – niece or full aunt – nephew (0.25), half uncle – niece or half aunt – nephew (0.125), full cousins (0.125), and half cousins (0.0625). The first three could be determined only when all 4 grandparents were known, which was the case for 917,465 pups born from 1999 onwards. The other relationships could be determined if all 8 great-grandparents were known, which was the case for 103,785 pups born from 2004 onwards.

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The effect of close relative matings on litter size. Close relative matings were grouped according to the relationship coefficient, resulting in 5 categories: no close relationship, 0.0625, 0.125, 0.25 and 0.5. Litters and litter sizes were determined by grouping pups with the same parents born at the same date. Only pups from the 13 most numerous breeds containing 47% of all registered dogs were analysed. This ensured that there were at least 20 animals in each relationship category, year and parity. The effects of relationship category, parity, year and interactions on litter size were determined in a 3-way ANOVA. The 13 breeds were supplemented with the Saarloos Wolfhond and Schapendoes breeds for which the breeding organisations provided detailed records over a longer period.

Inbreeding depression for litter size at population level in two breeds. The amount of maternal inbreeding depression for litter size was estimated for the databases of the Saarloos Wolfdog and Schapendoes provided by the breed clubs. These databases contained ancestry up to the start of the breeds in the 1940s. Only litters since the 1990s were used for the analysis, because before the 1990s sex ratios were skewed, suggesting that before the 1990s not all pups were registered but rather those that were later used for breeding. The following model was run with ASReml (Gilmour *et al.*, 2015):

$$LS_{ij} = u + Par_j + bF_i + A_i + Pe_i + e_{ij} \qquad (1)$$

with LS_{ij} being the number of registered pups (i.e. alive at 2 months of age) for the j^{th} litter of dam i, Par_j the parity of the litter, b the coefficient of regression of LS on the inbreeding coefficient F_i of the dam i, Ai the random genetic effect of dam i, Pe_i the random permanent environmental effect of the dam i across all her litters and e_{ij} the random residual.

Results

The frequency of close relative matings decreased over the years (Table 1). Father-daughter, Mother-son, Full sib and Grandparent – grandchild matings have not occurred since 2011.

Litter size was smaller in small-sized breeds, e.g. the Chihuahua with a mean of 2.7 pups, than in large-sized breeds, e.g. the Golden Retriever with a mean of 6.6 pups (Table 2). Differences between years were significant for 11 of the 15 breeds (Table 2), but only for the Saarloos Wolfdog there appeared to be a trend, with litter size decreasing from above 6 before the 1990s to 3.5 in 2008 after which it recovered to close to 5 pups.

Differences in litter sizes over all parities were significant in all breeds except the Saarloos Wolfdog. When compared to the mean litter size within breeds, litter size was on average 6% lower for first parity litters and 8% lower for parities above 4 (Figure 1). Differences in litter size between relationship categories were

Table 1. Percentage pups from close relative matings for all pedigreed pups registered in the Netherlands with known grandparents (1999 onwards) and with known great-grandparents (2004 onwards).

Years	Half Cousins	Full Cousins	Half uncle Niece	Full uncle Niece	Half Sibs	Grand parent g.child	Full Sibs	Parent Child
1999-2003	NA[1]	NA[1]	NA[1]	NA[1]	1.54%	NA[1]	0.17%	0.33%
2004-2008	11.03%	7.09%	9.07%	1.46%	1.38%	0.22%	0.09%	0.27%
2009-2013	8.05%	3.93%	7.19%	1.02%	0.83%	0.15%	0.03%	0.05%
2014-2018	6.95%	2.95%	6.17%	0.71%	0.60%	0.00%	0.00%	0.00%

[1] Not enough litters with great-grandparents known to determine percentage of matings.

Table 2. Analysed breeds, number of litters analysed, mean litter size and *P*-values for the effect of year, parity and relationship category on litter size in 3-way ANOVA.

Breed[1]	#Litter	Litter size (S.D)	Year	Parity	Relationship	Interactions[2]
LAB	13,808	6.3 (2.8)	0.000	0.000	0.053	
GSD	12,767	5.0 (2.8)	0.000	0.000	0.045	Y×P
DAH	12,742	3.9 (2.0)	0.000	0.000	0.000	P×R
GOR	7,486	6.6 (2.9)	0.004	0.000	0.000	
BMD	6,235	5.6 (2.9)	0.001	0.000	0.213	
BOX	5,327	4.9 (2.4)	0.018	0.000	0.502	
CKCS	5,638	3.7 (1.7)	0.001	0.000	0.820	
BCL	3,985	4.6 (2.6)	0.104	0.000	0.013	
BDF	3,076	5.9 (2.9)	0.067	0.000	0.102	
FBD	4,497	4.0 (2.2)	0.058	0.000	0.163	
CHI	6,629	2.7 (1.4)	0.000	0.000	0.048	
EBD	3,869	4.5 (2.5)	0.000	0.000	0.451	
ECS	3,703	4.6 (2.3)	0.161	0.000	0.030	Y×P, P×R
SWD	699	4.3 (2.6)	0.000	0.068	0.444	
SDS	4,643	5.9 (2.3)	0.000	0.000	0.000	

[1] LAB, Labrador Retriever; GSD, German Shepherd Dog; DAH, Dachshund; GOR, Golden Retriever; BMD, Bernese Mountain Dog; BOX, Boxer; CKCS, Cavalier King Charles Spaniel; BCL, Border Collie; BDF, Bouvier des Flandres; FBD, French Bulldog; CHI, Chihuahua; EBD, English Bulldog; ECS, English Cocker Spaniel; SWD, Saarloos Wolfdog; SDS, Schapendoes.

[2] Only significant interactions (*P*<0.05) are indicated.

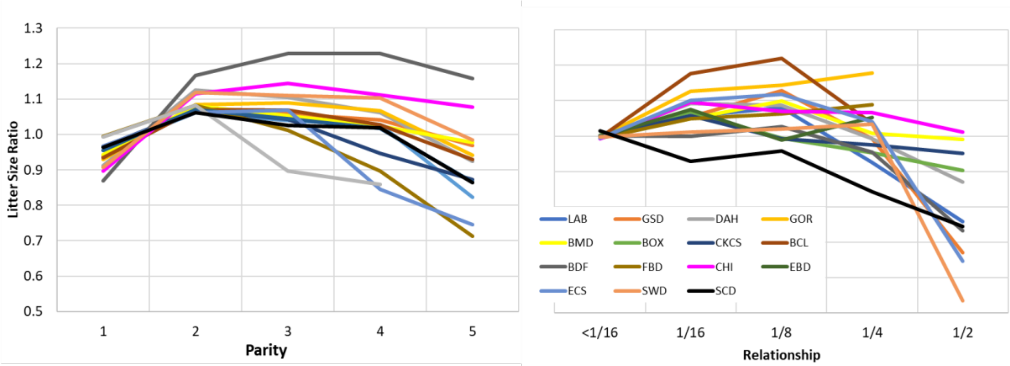

Figure 1. Litter size ratio (average within group litter size over breed average) over parity and relationship category. Breed abbreviations see Table 2.

significant for 7 of the 15 breeds. Litter size was on average 16% lower in the highest relationship category (Figure 1). Litter sizes were on average 8% higher for relationship category 0.0625 and 0.125.

Estimated heritabilities for litter size in the Saarloos Wolfdog and Schapendoes were moderate with 33 and 24% (Table 3). A 1% increase in the inbreeding coefficient of the mother resulted in an estimated reduction of litter size of 0.05 and 0.028 pups. This was equivalent to 1.16 and 0.47% of the trait mean, and 1.90 and 1.18% of the standard deviation.

Table 3. Genetic parameters (SE), inbreeding depression and *P*-value of effect maternal inbreeding for litter size in the Saarloos Wolfdog and Schapendoes.

Breed	V_A [1]	V_{PE} [2]	V_R [3]	h^2	+1% F [4]	p
Saarloos Wolfdog	2.16 (0.56)	0.47 (0.46)	3.96 (0.32)	0.327 (0.074)	-0.050	0.035
Schapendoes	1.29 (0.18)	0.56 (0.15)	3.61 (0.10)	0.236 (0.031)	-0.028	0.011

[1] Additive genetic variance.

[2] Permanent environmental variance.

[3] Residual variance, h^2 = heritability.

[4] Change in number of pups per 1% increase of inbreeding coefficient.

Discussion

The number of matings between closely related dogs clearly decreased over the years. This is probably due to increased awareness of the detrimental effects of inbreeding and in line with observations that the rate of inbreeding in most dog breeds have gone down (e.g. Lewis *et al.* 2015). The negative effect of inbreeding on litter size in individual matings was only evident for the highest relationship category (matings between full sibs or parent offspring), and only significant for about half of the breeds. For lower relatedness categories (0.0625 to 0.125) litter size was even above the breed's average for most breeds. Various studies have previously reported (insignificant) favourable effects of inbreeding in animal populations (e.g. Doekes *et al.*, 2021). Apparently, the effect of inbreeding depression, when present, is so small that it could be masked by other factors. When the effect of maternal inbreeding was analysed at the population level it was highly significant for both breeds. Leroy *et al.* (2015) found clear inbreeding depression as well, with similar analyses as in this paper in seven breeds, and of similar size (0.007 to 0.042 per 1% F) as we found (0.028 and 0.050). One advantage of genetic analysis at the population level is that genetic effects other than inbreeding can be taken into account as well. Selective breeding, e.g. mating dogs from large litters to each other, may for example lead to relatively large litters for more inbred litters. For breeders and owners that have to select mates for their dogs, it is thus important to avoid mating closely related dogs. The effect of mating less related dogs is less obvious. Genetic management of breeds is, however, important to prevent a permanent reduction in litter size due to fixation of genetic defects with small effect due to genetic drift, i.e. an imbalance between inbreeding rate and selection/purging. The reduction in litter size as observed in the Saarloos Wolfhond may well have been the result of its high inbreeding rate over a long time.

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