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Canine perinatal mortality: A cohort study of 224 breeds

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Abstract

Canine perinatal mortality is known to be relatively high. However, the literature on perinatal mortality in dogs is still sparse and often refers to a single or only a few breeds. The aim of this large-scale observational study was to describe the perinatal mortality in purebred dogs of various breeds at both puppy and litter level. In addition, the influence of breed, breed size, litter size, age of the bitch, litter number and season for whelping on the risk of perinatal mortality at litter level was studied and the mean litter size at eight days and eight wks after birth was calculated. A retrospective cohort study was performed by studying 10,810 litters of 224 breeds registered in the Norwegian Kennel Club in 2006 and 2007. Perinatal mortality was defined as the sum of stillborn puppies and puppies that died during the first wk after birth (early neonatal mortality) and was present in 24.6% of the litters. Eight percent of the puppies died before eight days after birth, with 4.3% as stillbirth and 3.7% as early neonatal mortality. For most breeds the perinatal mortality was low, but for some breeds a higher perinatal mortality was found. The mean litter size at eight days and eight wks after birth was 4.97 (±0.02) and 4.92 (±0.02) puppies, respectively. Of all puppies born, only 1% died during the period from eight days to eight wks after birth. Random effects logistic regression analysis indicated that increasing litter size and age of the bitch were associated with an increased risk of stillbirth, early neonatal mortality and total perinatal mortality at the litter level ($P < 0.001$). The random breed effect was significant for all outcomes. Litter number also had a significant effect on stillbirth, early neonatal mortality and total perinatal mortality at the litter level, with the highest risk of perinatal mortality found in the first litter ($P < 0.001$). Further, the risk of early neonatal mortality was doubled in litters with stillborn puppies. No significant effect of whelping season on perinatal mortality at litter level was found. An interaction existed between the age of the bitch and litter number and the risk of stillbirth was three times as high (odds ratio = 3.00) in litters from bitches having their first litter after the age of six y. Breed was a more important determinant of perinatal mortality in litters than breed size. However, more than 90% of the variation in perinatal mortality was found at the individual litter level and efforts to minimize puppy mortality should be targeted at the management of the individual litter rather than at the breed level.

Keywords: Dogs; Puppies; Stillbirth; Neonatal mortality; Risk factors; Mortality risk

1. Introduction

Perinatal mortality is the number of fetal or neonatal deaths around birth. In humans, perinatal mortality is defined as the sum of fetal losses, or stillbirths, and neonatal losses. The neonatal mortality can be divided into early and late neonatal mortality, the first being deaths within the first seven days of life and the latter being deaths that occur from seven to 28 days after birth [1]. The length of the canine neonatal period has no universally accepted definition, but is usually lim-

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ited to the first two to three wk of life [2,3]. One definition of canine perinatal mortality is the combined loss because of stillbirths and early neonatal mortality, where early neonatal mortality includes live-born puppies that die within the first seven days after birth [4].

Canine perinatal mortality is known to be relatively high, and the loss of puppies peaks around birth and during the first wk of life [3–9]. Puppies are born physiologically immature and totally dependent of their mother [10]. The causes for the high puppy mortality in the perinatal period are complex and can relate to several factors concerning the bitch (mismothering, lack of milk, trauma), the birth process (prolonged labor, dystocia, obstetrics), the puppy (low birth weight, congenital malformations, starvation), the environment and to the presence of infectious agents [3,4,7,8,10,11]. However, fetal asphyxia and bacterial infections are thought to be among the most common causes of perinatal death in dogs [4,10,12]. In some breeds, healthy puppies that do not meet the breed standard because of e.g. wrong coat color or coat pattern are regularly euthanized. This contributes to the perinatal losses in many countries [4,6].

The first studies of canine perinatal mortality were based on registrations from dogs in breeding colonies that were produced for research purposes [8,9,13,14]. More recently, studies have been performed among dogs kept as pets with information being collected from breeders through questionnaires [3–6]. However, the literature on perinatal mortality is still relatively sparse and often refers to a single [8] or a limited number [3] of breeds.

Variation in perinatal mortality exists between breeds. In a Beagle breeding colony, the proportion of puppies lost because of perinatal mortality was 12.9% [8], while a proportion of 16.9% was found in a Norwegian cohort study of four large breeds [3]. In the few existing studies of various breeds, the perinatal mortality ranged from 18.5% [4] to 26.3% [5]. Stillbirth proportions of 2.2% in the Foxhound [7], 4.6% in the Beagle [8], 5.6% in the Boxer [6] and 7.2% in the German Shepherd [12] have been reported. Further, a study of Irish Wolfhound, Leonberger, Labrador Retriever and Newfoundland found 10.9% stillborn puppies [3], while 6.5% [5] and 7% [4] were reported from other studies including several breeds.

Large-scale epidemiological studies on canine perinatal mortality are needed to get a more complete understanding of the risk of perinatal mortality in the dog as a species. Breed-specific information on perinatal mortality is still lacking for the majority of dog breeds and will be valuable for both breeders and veterinarians.

Perinatal mortality can be analyzed at the puppy level, where the outcome variable is the number, or proportion of dead puppies. This measure will be influenced by the number of puppies born per litter which will also vary by breed. Alternatively, the number or proportion of litters which contain dead puppies can be calculated and this can be defined as perinatal mortality at the litter level. Incidence risk is the probability that an individual will develop a disease in a defined period, and can be calculated for closed populations where the individual is observed for the full risk period [15]. If the disease event of interest is death, the term mortality risk should be used.

More than 90% of all purebred dogs in Norway are registered in the Norwegian Kennel Club (NKC) [16]. For each litter that is registered by breeders in the NKC, information about the dam, sire and litter is stored in a database. Based on these registrations from 2006 and 2007, a large study on canine litter size and perinatal mortality was initiated. The first part of the study focused on litter size at birth [17]. Here, the second part of the study is presented with the aim to describe the perinatal mortality risk during the first wk of life in the Norwegian population of purebred dogs at puppy and litter level, and to study whether age of the bitch, litter number, litter size, breed, breed size and season of whelping influence the risk of perinatal mortality at litter level.

2. Materials and methods

2.1. Study population

A cohort study was performed, including data from the time of birth for all purebred litters registered by breeders in the NKC from January 1st, 2006 to December 31st, 2007.

2.2. Data collection

It is mandatory for breeders to fill in a questionnaire when registering a litter in the NKC. For the dam and sire of the litter, breed, names and NKC registration numbers are reported by the breeders. The birthdate of the litter, the number of live and stillborn puppies as well as the number of puppies alive seven days post partum are also reported. These electronically stored data were received from the NKC. A database was established in Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA), and extensively quality

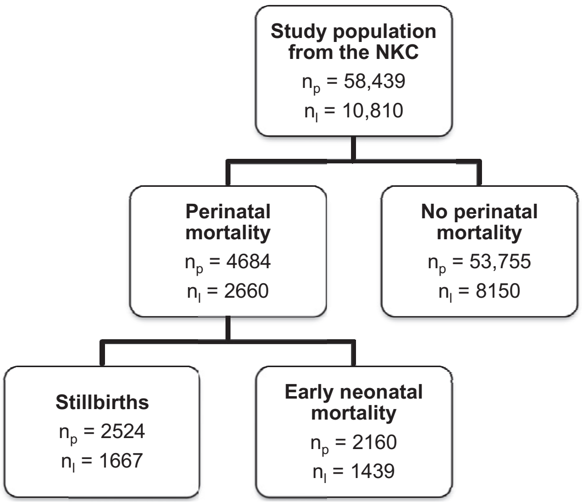

Fig. 1. Perinatal mortality at puppy (n_p = number of puppies) and litter level (n_l = number of litters) in litters registered in the Norwegian Kennel Club (NKC) during 2006 and 2007. In 446 of the litters, both stillbirth and early neonatal mortality occurred.

assured by excluding duplicates and litter registrations with incomplete information for the analysis (n = 181). Litters in which all the puppies died are not reported to the NKC by the breeders and therefore not included in the study.

2.3. Definitions

Outcome and explanatory variables were defined from the information in the dataset. A visual presentation of some of the terms in this section is given in Fig. 1.

Stillbirth: Stillborn puppies were puppies reported as dead at birth by the breeder. The individual risk of stillbirth was calculated, as well as the risk of a litter containing at least one stillborn puppy.

Early neonatal mortality: The number of puppies that died during the first seven days after birth (early neonatal mortality) was calculated by subtracting the number of puppies alive seven days after birth from the number of live-born puppies. The risk of early neonatal mortality was calculated by dividing the number of puppies that died during the first seven days after birth by the total number of puppies born. Early neonatal mortality risk is presented at puppy and litter level.

Perinatal mortality: Perinatal mortality risk was calculated by dividing the sum of dead puppies because of stillbirth and early neonatal mortality during the first seven days of life by the total number of born puppies, and is presented at the individual puppy level and at the litter level.

Litter size: Litter size at birth was defined as the sum of live-born and stillborn puppies and has been described and analyzed more extensively elsewhere [17]. Here, mean litter size at eight days after birth, as well as mean litter size at the time of official registration of puppies in the NKC (approximately eight wks of age) was calculated for each breed.

Breed and breed size: Because the database did not contain information about the body weight of the individual dog, the mean body weight of each breed was estimated from the midpoint of the body weight interval for female and male dogs based on the breed standard. The body weight intervals were collected from Fédération Cynologique Internationale (FCI) [18], the Kennel Club in the UK [19], from breed literature and from breed clubs. All breeds were then classified into one of the five following breed size groups: Miniature breeds (<5 kg), small breeds (5–10 kg), medium breeds (10–25 kg), large breeds (25–45 kg) and giant breeds (>45 kg).

Age of the bitch: The age of the bitch at the time of whelping was obtained in days by subtracting the birthdate of the litter from the birthdate of the bitch. The age in days was converted into y: <one y = 0 - 364 days, one y = 365 to 729 days, two y =730 to 1094 days and so on.

Litter number: Litter number, or parity, was defined as the total number of litters born by the bitch. Bitches registered with four litters or more were grouped together in the random-effects logistic models because of the small number of observations.

Season: To study potential effects of whelping season on perinatal mortality at litter level, the litters were grouped according to birth month (1 = January, 2 = February and so on) and a categorical variable called "season" was created, where spring = February–April, summer = May–July, fall = August–October and winter = November–January. This particular division was chosen to reflect the climatic conditions in Norway and to obtain four equally sized groups for the analysis.

2.4. Statistical analysis

Descriptive statistics and multivariable analysis were performed using the software package Stata Version 11.0 (Stata Corporation, College Station, Tex., USA).

2.4.1. Descriptive statistics

The risk of stillbirth, early neonatal mortality and total perinatal mortality was calculated at puppy and litter level for the study population as a whole and for each breed included in the study. Descriptive statistics for perinatal mortality in relation to the predictors; breed size group, litter size, litter number (parity), season of birth and age of the bitch were also produced at puppy and litter level for the entire study population. The 95% confidence intervals for the proportion of dead puppies lost by category were calculated based on standard errors (SE) from a Poisson distribution. The median and range of puppies lost are presented by breed.

2.4.2. Multivariable methods

Three litter level logistic regression models were fitted, where the outcome variables were: stillbirth (0/1), early neonatal mortality (0/1) and any perinatal mortality (0/1). The size of the litter was included in the analysis by adding ln (litter size) as the offset in all three models. In the model for early neonatal mortality, stillbirth in the litter was also evaluated as a predictor in the analysis. Initial screening of the predictors was performed using univariable logistic regression and applying a liberal P value (0.1) for retaining a variable in the analysis. The assumption of linearity for continuous predictors was tested by categorizing the variable and computing the log odds of the outcome in each category against the midpoint of the category. The final models were created through manual backwards elimination, with a cut-off of $P = 0.05$ for keeping variables in the model. Overall significance of groups of variables, e.g. season and litter number, was tested using likelihood-ratio (LR) tests. Breed was included in the final model as a random effect, to account for the lack of independence between observations from litters within the same breed. The significance of adding the random effect for breed compared to ordinary logistic regression was tested using an LR test. All possible two-way interactions were tested between predictors retained in the final models. Pearson and standardized residuals were utilized to evaluate model-fit at the litter and breed level [20].

3. Results

3.1. Study population

A total of 10,810 litters (= n_l) with 58,439 puppies (= n_p) of 224 breeds were included in the final database (Fig. 1). Most of the bitches, 7502 individuals (82.2%), contributed one litter each in the period from 2006 to 2007, 1564 individuals (17.1%) gave birth to two litters, whereas 60 (0.66%) bitches mothered three litters in this period. Lack of independence between litters born by the same bitch was ignored for the purpose of the analysis, where the litter was the unit of observation. Of the 224 breeds, 61.2% (n = 137) had 10 or more litters registered in the database. Perinatal mortality was present in 82.6% (n = 185) of the breeds. For all 224 breeds, descriptive statistics of stillbirth, early neonatal mortality and total perinatal mortality risks at puppy and litter level are presented in Supplementary File 1, together with the mean litter size at eight days and eight wks after birth. In the following, descriptive results for puppy level mortality will be presented separately and followed by descriptive statistics and results from the multivariable analysis at the litter level.

3.2. Perinatal mortality at puppy level

The overall perinatal mortality risk in puppies was 8.0% (n_p = 4684) with 4.3% (n_p = 2524) of deaths caused by stillbirth and 3.7% (n_p = 2160) by early neonatal mortality (Table 1, Fig. 1). In the whole study population, the number of puppies lost per litter because of perinatal mortality ranged from 0 to 16. The number of puppies alive at eight days and registered at eight wks of age was 53,755 and 53,175, respectively, which gave a total puppy loss of 9.0%

Table 1
Perinatal mortality risks with 95% confidence intervals (CI) in 10,810 litters with 58,439 puppies from 224 dog breeds. n_p = number of puppies, n_l = number of litters.

	Puppy level Median per litter					Litter level		
	n_p	%	95% CI	Range		n_l	%	95% CI
Stillbirth	2524	4.3	4.1, 4.5	0–10	0	1667	15.4	14.7, 16.2
Early neonatal mortality	2160	3.7	3.5, 3.9	0–10	0	1439	13.3	12.6, 14.0
Perinatal mortality	4684	8.0	7.8, 8.2	0–16	0	2660*	24.6	23.7, 25.6
No perinatal mortality	53,755	92.0	91.2, 92.8	—	—	8150	75.4	73.8, 77.0

* In 446 of the litters, both stillbirth and early neonatal mortality were present.

($n_p = 5264$) from birth to the time of official registration in the NKC (approximately eight wks of age). Of all puppy losses that occurred in this period, 89% was caused by perinatal mortality (stillbirths and early neonatal mortality).

3.2.1. Breed

The perinatal mortality risk varied with breed. The popularity of the breeds was determined by the total number of litters registered in NKC from 2006 to 2007. An overview of the perinatal mortality risk at puppy level for the 100 most popular breeds in the study population is given in Table 2 and further information is available in Supplementary File 1.

Among the 100 most popular breeds, the highest total perinatal mortality risk at the individual puppy level of 24.6% (52/211) was found in the Dogue de Bordeaux. This was followed by 19.5% (75/385) in the Dalmatian, 17.9% (48/268) among Rhodesian Ridgebacks and 17.0% (86/507) in the Pug. In contrast, the lowest perinatal mortality risk was found in the Basenji with 0% (0/106) followed by 0.9% (1/112) in the Italian Greyhound, 1.4% (2/146) in the Tibetan Terrier, 1.5% (5/333) among Irish Soft Coated Wheaten Terriers and 1.6% (5/315) in the Bichon Havanaise.

Dogue de Bordeaux also had the highest risk of stillbirth at the individual puppy level of 14.2% (30/211), and was followed by 12.3% (38/308) stillbirth in the St. Bernard, 12.1% (19/157) in the Chow Chow, 11.7% (18/154) among Welsh Corgis (Pembroke) and 10.6% (41/385) in the Dalmatian. Neither the Basenji (0/106), the Italian Greyhound (0/112) or the Australian Terrier (0/122) had stillborn puppies, while a low proportion of 0.6% stillbirth was found in the Irish Soft Coated Wheaten Terrier (2/333) and the Bichon Havanaise (2/315).

The highest early neonatal mortality risk of 11.6% (31/268) was found in the Rhodesian Ridgeback and was followed by 10.4% (22/211) in the Dogue de Bordeaux, 8.8% (34/385) among Dalmatians and 8.7% (9/104) in the Icelandic Sheepdog. In contrast, both the Basenji (0/106) and the Tibetan Terrier (0/146) had no early neonatal mortality. In the Border Terrier (1/138) and the Danish-Swedish Farmdog (1/148) 0.7% early neonatal mortality was found.

3.2.2. Breed size

The overall proportion of stillborn puppies ranged from 2.6% in miniature breeds to 6.7% in giant breeds. The proportion of early neonatal mortality in puppies ranged from 3.3% in miniature breeds to 3.7% in large breeds, while the giant breeds had an overall early neonatal mortality in puppies of 4.9%. The total perinatal mortality risk for individual puppies was 5.9% in miniature breeds, 7.3% in both small and medium breeds, 8.8% in large breeds and 11.6% in giant breeds (Table 3).

3.2.3. Litter size

The highest perinatal mortality risk in puppies (19.9%) was found in litters with 12 puppies or more. In contrast, the lowest mean perinatal mortality risk (6.0%) was found in litters with seven puppies (Table 4).

3.2.4. Age of the bitch and litter number

When describing the relationship between the age of the bitch and perinatal mortality, eight y old bitches had the highest proportion of dead puppies (13.4%), while the lowest (7.1%) was found in two y old bitches (Table 5). The first litter of the bitch had the highest perinatal mortality risk for puppies (8.5%) (Table 6).

3.3. Perinatal mortality at litter level

Perinatal mortality occurred in 24.6% ($n_l = 2660$) of the 10,810 litters (Fig. 1, Table 1). Stillbirth was present in 11.3% ($n_l = 1221$) of the litters exclusively, while 9.2% ($n_l = 993$) of the litters experienced early neonatal mortality, exclusively. In 4.1% ($n_l = 446$) of all litters registered, both stillbirth and early neonatal mortality occurred. In the whole study population, the mean litter size at eight days after birth was 4.97 (± 0.02) puppies, compared to 5.4 at birth [17], whereas at eight wks after birth, the mean litter size was 4.92 (± 0.02).

3.3.1. Breed

Also at litter level, variations in the perinatal mortality risk existed between breeds (Table 2). The highest risk of perinatal mortality in litters was found in the Dogue de Bordeaux, with 69.2% (18/26) of the litters having stillborn puppies and/or puppies dying the first wk after birth. This was followed by 63.0% (29/46) 58.6% (17/29) and 56.7% (17/30) in the Dalmatian, the Great Dane and the Rhodesian Ridgeback, respectively. The Basenji had no perinatal mortality (0/22) during the first wk of life in this material, while low risks of mortality of 2.9% (1/34), 5.5% (4/73) and 5.7% (2/35) were found in the Italian Greyhound, the Bichon Havanaise and the Danish-Swedish Farmdog, respectively.

In the Dogue de Bordeaux, stillbirth was found in 57.7% (15/26) of the litters followed by 47.8% (22/In the Dogue de Bordeaux, stillbirth was found in 57.7% (15/26)

Table 2
Perinatal mortality risk at puppy and litter level in the 100 most popular dog breeds, determined by the total number of litters registered in the Norwegian Kennel Club in 2006 and 2007. For each outcome variable, median and range are given in Supplementary File 1.

Breed	Puppy level				Litter level				
	Puppies n_p	Stillbirth n_p (%)	ENM n_p (%)	PNM n_p (%)	Litters n_l	Stillbirth n_l (%)	ENM n_l (%)	PNM n_l (%)	Mean litter size Day 8 (± SEM)
Alaskan Malamute	339	16 (4.7)	9 (2.7)	25 (7.4)	49	11 (22.4)	5 (10.2)	15 (30.6)	6.4 (0.3)
Am. Cocker Spaniel	508	18 (3.5)	19 (3.7)	37 (7.3)	95	15 (15.8)	13 (13.7)	24 (25.3)	5.0 (0.2)
Australian Terrier	122	0 (0.0)	6 (4.9)	6 (4.9)	22	0 (0.0)	4 (18.2)	4 (18.2)	5.3 (0.4)
Basenji	106	0 (0.0)	0 (0.0)	0 (0.0)	22	0 (0.0)	0 (0.0)	0 (0.0)	4.8 (0.4)
Basset Hound	140	7 (5.0)	6 (4.3)	13 (9.3)	21	5 (23.8)	4 (19.0)	7 (33.3)	6.0 (0.7)
Beagle	623	35 (5.6)	20 (3.2)	55 (8.8)	113	23 (20.4)	15 (13.3)	30 (26.5)	5.0 (0.2)
Belgian Shepherd Dog (Groenendael)	183	3 (1.6)	13 (7.1)	16 (8.7)	29	3 (10.3)	4 (13.8)	5 (17.2)	5.8 (0.3)
Belgian Shepherd Dog (Tervueren)	323	8 (2.5)	5 (1.5)	13 (4.0)	52	8 (15.4)	3 (5.8)	10 (19.2)	6.0 (0.3)
Bernese Mountain Dog	878	73 (8.3)	25 (2.8)	98 (11.2)	137	51 (37.2)	15 (10.9)	59 (43.1)	5.7 (0.2)
Bichon Frise	883	15 (1.7)	22 (2.5)	37 (4.2)	192	13 (6.8)	16 (8.3)	24 (12.5)	4.4 (0.1)
Bichon Havanais	315	2 (0.6)	3 (1.0)	5 (1.6)	73	2 (2.7)	3 (4.1)	4 (5.5)	4.2 (0.2)
Border Collie	1939	89 (4.6)	84 (4.3)	173 (8.9)	323	56 (17.3)	51 (15.8)	94 (29.1)	5.5 (0.1)
Border Terrier	138	7 (5.1)	1 (0.7)	8 (5.8)	27	6 (22.2)	1 (3.7)	7 (25.9)	4.8 (0.4)
Boston Terrier	187	12 (6.4)	14 (7.5)	26 (13.9)	46	11 (23.9)	11 (23.9)	19 (41.3)	3.5 (0.3)
Boxer	916	20 (2.2)	19 (2.1)	39 (4.3)	139	19 (13.7)	11 (7.9)	28 (20.1)	6.3 (0.2)
Brittany	339	10 (2.9)	7 (2.1)	17 (5.0)	53	6 (11.3)	3 (5.7)	9 (17.0)	6.1 (0.3)
Bull Terrier	199	4 (2.0)	6 (3.0)	10 (5.0)	36	4 (11.1)	3 (8.3)	5 (13.9)	5.3 (0.4)
Bulldog	199	3 (1.5)	14 (7.0)	17 (8.5)	37	1 (2.7)	11 (29.7)	11 (29.7)	4.9 (0.5)
Cairn Terrier	807	31 (3.8)	13 (1.6)	44 (5.5)	182	23 (12.6)	13 (7.1)	34 (18.7)	4.2 (0.1)
Cavalier King Charles Spaniel	1819	77 (4.2)	58 (3.2)	135 (7.4)	439	48 (10.9)	41 (9.3)	78 (17.8)	3.8 (0.1)
Chihuahua	850	32 (3.8)	36 (4.2)	68 (8.0)	269	30 (11.2)	31 (11.5)	55 (20.4)	2.9 (0.1)
Chinese Crested	569	18 (3.2)	24 (4.2)	42 (7.4)	133	17 (12.8)	17 (12.8)	28 (21.1)	4.0 (0.1)
Chow Chow	157	19 (12.1)	6 (3.8)	25 (15.9)	36	11 (30.6)	6 (16.7)	15 (41.7)	3.7 (0.4)
Cocker Spaniel	991	24 (2.4)	64 (6.5)	88 (8.9)	174	15 (8.6)	39 (22.4)	46 (26.4)	5.2 (0.1)
Collie (rough)	526	31 (5.9)	31 (5.9)	62 (11.8)	101	24 (23.8)	20 (19.8)	35 (34.7)	4.6 (0.2)
Coton de Tulear	103	4 (3.9)	1 (1.0)	5 (4.9)	27	3 (11.1)	1 (3.7)	3 (11.1)	3.6 (0.2)
Dachshund	1941	33 (1.7)	69 (3.6)	102 (5.3)	358	30 (8.4)	52 (14.5)	72 (20.1)	5.1 (0.1)
Dachshund (miniature)	636	17 (2.7)	17 (2.7)	34 (5.3)	144	12 (8.3)	12 (8.3)	21 (14.6)	4.2 (0.1)
Dachshund (rabbit)	114	1 (0.9)	6 (5.3)	7 (6.1)	35	1 (2.9)	6 (17.1)	7 (20.0)	3.1 (0.2)
Dalmatian	385	41 (10.6)	34 (8.8)	75 (19.5)	46	22 (47.8)	20 (43.5)	29 (63.0)	6.7 (0.4)
Danish-Swedish Farmdog	148	2 (1.4)	1 (0.7)	3 (2.0)	35	1 (2.9)	1 (2.9)	2 (5.7)	4.1 (0.3)
Dobermann	316	19 (6.0)	15 (4.7)	34 (10.8)	45	12 (26.7)	8 (17.8)	18 (40.0)	6.3 (0.4)
Dogue de Bordeaux	211	30 (14.2)	22 (10.4)	52 (24.6)	26	15 (57.7)	10 (38.5)	18 (69.2)	6.1 (0.5)
English Setter	1702	52 (3.1)	54 (3.2)	106 (6.2)	266	36 (13.5)	38 (14.3)	65 (24.4)	6.0 (0.1)
English Springer Spaniel	539	23 (4.3)	15 (2.8)	38 (7.1)	74	19 (25.7)	13 (17.6)	24 (32.4)	6.8 (0.2)
Eurasier	147	6 (4.1)	2 (1.4)	8 (5.4)	22	3 (13.6)	2 (9.1)	4 (18.2)	6.3 (0.6)
Finnish Hound	526	39 (7.4)	31 (5.9)	70 (13.3)	74	25 (33.8)	15 (20.3)	34 (45.9)	6.2 (0.3)
Finnish Lapphund	124	2 (1.6)	4 (3.2)	6 (4.8)	24	2 (8.3)	3 (12.5)	5 (20.8)	4.9 (0.3)
Finnish Spitz	85	7 (8.2)	6 (7.1)	13 (15.3)	23	5 (21.7)	5 (21.7)	9 (39.1)	3.1 (0.2)
Flat Coated Retriever	997	42 (4.2)	40 (4.0)	82 (8.2)	120	27 (22.5)	29 (24.2)	48 (40.0)	7.6 (0.3)
French Bulldog	165	8 (4.8)	13 (7.9)	21 (12.7)	35	8 (22.9)	8 (22.9)	12 (34.3)	4.1 (0.3)
German Shepherd Dog	2848	155 (5.4)	91 (3.2)	246 (8.6)	465	94 (20.2)	59 (12.7)	129 (27.7)	5.6 (0.1)
German Shorthaired Pointer	533	34 (6.4)	17 (3.2)	51 (9.6)	64	21 (32.8)	12 (18.8)	28 (43.8)	7.5 (0.4)
German Wirehaired Pointer	386	22 (5.7)	14 (3.6)	36 (9.3)	53	11 (20.8)	8 (15.1)	17 (32.1)	6.6 (0.4)
Giant Schnauzer	293	14 (4.8)	6 (2.0)	20 (6.8)	42	10 (23.8)	6 (14.3)	13 (31.0)	6.5 (0.5)
Golden Retriever	2189	135 (6.2)	57 (2.6)	192 (8.8)	291	86 (29.6)	38 (13.1)	105 (36.1)	6.9 (0.2)
Gordon Setter	1659	69 (4.2)	53 (3.2)	122 (7.4)	219	38 (17.4)	26 (11.9)	53 (24.2)	7.0 (0.2)
Great Dane	205	19 (9.3)	11 (5.4)	30 (14.6)	29	11 (37.9)	9 (31.0)	17 (58.6)	6.0 (0.6)
Greenland Dog	200	7 (3.5)	19 (9.5)	26 (13.0)	36	6 (16.7)	9 (25.0)	14 (38.9)	4.8 (0.4)
Hamilton Hound	155	5 (3.2)	6 (3.9)	11 (7.1)	24	4 (16.7)	3 (12.5)	5 (20.8)	6.0 (0.5)
Icelandic Sheepdog	104	7 (6.7)	9 (8.7)	16 (15.4)	23	5 (21.7)	6 (26.1)	10 (43.5)	3.8 (0.3)
Irish Setter	1036	28 (2.7)	24 (2.3)	52 (5.0)	145	18 (12.4)	19 (13.1)	32 (22.1)	6.8 (0.2)
Irish Soft Coated Wheaten Terrier	333	2 (0.6)	3 (0.9)	5 (1.5)	57	2 (3.5)	3 (5.3)	4 (7.0)	5.8 (0.2)

Table 2
Continued

Breed	Puppy level				Litter level				
	Puppies n_p	Stillbirth n_p (%)	ENM n_p (%)	PNM n_p (%)	Litters n_l	Stillbirth n_l (%)	ENM n_l (%)	PNM n_l (%)	Mean litter size Day 8 (± SEM)
Italian Greyhound	112	0 (0.0)	1 (0.9)	1 (0.9)	34	0 (0.0)	1 (2.9)	1 (2.9)	3.3 (0.3)
Jack Russel Terrier	613	14 (2.3)	12 (2.0)	26 (4.2)	138	13 (9.4)	10 (7.2)	18 (13.0)	4.3 (0.1)
Japanese Spitz	355	6 (1.7)	3 (0.8)	9 (2.5)	91	5 (5.5)	3 (3.3)	7 (7.7)	3.8 (0.1)
Labrador Retriever	1549	103 (6.6)	78 (5.0)	181 (11.7)	223	59 (26.5)	41 (18.4)	88 (39.5)	6.1 (0.2)
Lagotto Romagnolo	173	3 (1.7)	3 (1.7)	6 (3.5)	26	3 (11.5)	2 (7.7)	4 (15.4)	6.4 (0.3)
Leonberger	388	21 (5.4)	33 (8.5)	54 (13.9)	46	14 (30.4)	16 (34.8)	24 (52.2)	7.3 (0.5)
Lhasa Apso	168	4 (2.4)	4 (2.4)	8 (4.8)	34	3 (8.8)	4 (11.8)	7 (20.6)	4.7 (0.3)
Manchester Terrier	98	1 (1.0)	3 (3.1)	4 (4.1)	21	1 (4.8)	3 (14.3)	4 (19.0)	4.5 (0.3)
Miniature Pinscher	323	4 (1.2)	6 (1.9)	10 (3.1)	76	4 (5.3)	4 (5.3)	8 (10.5)	4.1 (0.2)
Miniature Schnauzer	963	31 (3.2)	30 (3.1)	61 (6.3)	205	25 (12.2)	25 (12.2)	46 (22.4)	4.4 (0.1)
Newfoundland	370	21 (5.7)	20 (5.4)	41 (11.1)	57	15 (26.3)	12 (21.1)	23 (40.4)	5.8 (0.4)
Norfolk Terrier	62	5 (8.1)	3 (4.8)	8 (12.9)	25	4 (16.0)	3 (12.0)	6 (24.0)	2.2 (0.2)
Norwegian Buhund	177	3 (1.7)	4 (2.3)	7 (4.0)	36	3 (8.3)	3 (8.3)	6 (16.7)	4.7 (0.3)
Norwegian Elkhound (Black)	340	22 (6.5)	18 (5.3)	40 (11.8)	65	19 (29.2)	11 (16.9)	24 (36.9)	4.6 (0.2)
Norwegian Elkhound (Grey)	2154	75 (3.5)	83 (3.9)	158 (7.3)	390	54 (13.8)	58 (14.9)	97 (24.9)	5.1 (0.1)
Norwegian Hound (Dunker)	303	23 (7.6)	18 (5.9)	41 (13.5)	41	10 (24.4)	10 (24.4)	13 (31.7)	6.4 (0.5)
Norwegian Lundehund	147	5 (3.4)	6 (4.1)	11 (7.5)	46	4 (8.7)	4 (8.7)	7 (15.2)	3.0 (0.2)
Nova Scotia Duck Tolling Retriever	486	14 (2.9)	9 (1.9)	23 (4.7)	74	12 (16.2)	6 (8.1)	17 (23.0)	6.3 (0.2)
Papillon	550	15 (2.7)	27 (4.9)	42 (7.6)	166	13 (7.8)	23 (13.9)	31 (18.7)	3.1 (0.1)
Petit Basset Griffon Vendéen	177	12 (6.8)	7 (4.0)	19 (10.7)	35	8 (22.9)	5 (14.3)	12 (34.3)	4.5 (0.3)
Phaléne	142	4 (2.8)	5 (3.5)	9 (6.3)	43	4 (9.3)	5 (11.6)	7 (16.3)	3.1 (0.2)
Pointer	595	23 (3.9)	15 (2.5)	38 (6.4)	83	17 (20.5)	13 (15.7)	25 (30.1)	6.7 (0.3)
Pomeranian	423	10 (2.4)	14 (3.3)	24 (5.7)	179	8 (4.5)	12 (6.7)	20 (11.2)	2.2 (0.1)
Poodle (medium)	390	7 (1.8)	14 (3.6)	21 (5.4)	105	6 (5.7)	10 (9.5)	14 (13.3)	3.5 (0.2)
Poodle (miniature)	448	11 (2.5)	11 (2.5)	22 (4.9)	151	9 (6.0)	7 (4.6)	15 (9.9)	2.8 (0.1)
Poodle (standard)	721	18 (2.5)	12 (1.7)	30 (4.2)	103	11 (10.7)	10 (9.7)	19 (18.4)	6.7 (0.2)
Poodle (toy)	236	6 (2.5)	7 (3.0)	13 (5.5)	100	6 (6.0)	6 (6.0)	12 (12.0)	2.2 (0.1)
Pug	507	45 (8.9)	41 (8.1)	86 (17.0)	120	34 (28.3)	28 (23.3)	49 (40.8)	3.5 (0.1)
Rhodesian Ridgeback	268	17 (6.3)	31 (11.6)	48 (17.9)	30	11 (36.7)	11 (36.7)	17 (56.7)	7.3 (0.4)
Rottweiler	1583	62 (3.9)	64 (4.0)	126 (8.0)	214	34 (15.9)	35 (16.4)	60 (28.0)	6.8 (0.2)
Samoyed	253	20 (7.9)	15 (5.9)	35 (13.8)	41	10 (24.4)	12 (29.3)	17 (41.5)	5.3 (0.4)
Schnauzer	195	8 (4.1)	5 (2.6)	13 (6.7)	28	6 (21.4)	3 (10.7)	8 (28.6)	6.5 (0.5)
Shetland Sheepdog	1143	58 (5.1)	74 (6.5)	132 (11.5)	292	43 (14.7)	57 (19.5)	89 (30.5)	3.5 (0.1)
Shiba Inu	138	2 (1.4)	3 (2.2)	5 (3.6)	42	2 (4.8)	3 (7.1)	5 (11.9)	3.2 (0.3)
Shih Tzu	398	8 (2.0)	23 (5.8)	31 (7.8)	95	7 (7.4)	15 (15.8)	20 (21.1)	3.9 (0.2)
Siberian Husky	450	19 (4.2)	6 (1.3)	25 (5.6)	88	8 (9.1)	6 (6.8)	14 (15.9)	4.8 (0.2)
Small Munsterlander	165	15 (9.1)	3 (1.8)	18 (10.9)	24	7 (29.2)	3 (12.5)	10 (41.7)	6.1 (0.5)
St. Bernard	308	38 (12.3)	14 (4.5)	52 (16.9)	45	12 (26.7)	7 (15.6)	16 (35.6)	5.7 (0.4)
Staffordshire Bull Terrier	460	27 (5.9)	11 (2.4)	38 (8.3)	82	19 (23.2)	8 (9.8)	24 (29.3)	5.1 (0.2)
Swedish Dachsbracke (Drever)	516	17 (3.3)	7 (1.4)	24 (4.7)	84	12 (14.3)	7 (8.3)	17 (20.2)	5.9 (0.3)
Swedish Elkhound (Jämthund)	527	34 (6.5)	13 (2.5)	47 (8.9)	70	15 (21.4)	9 (12.9)	22 (31.4)	6.9 (0.3)
Tibetan Spaniel	1179	24 (2.0)	43 (3.6)	67 (5.7)	312	21 (6.7)	31 (9.9)	45 (14.4)	3.6 (0.1)
Tibetan Terrier	146	2 (1.4)	0 (0.0)	2 (1.4)	28	2 (7.1)	0 (0.0)	2 (7.1)	5.1 (0.3)
Welsh Corgi (Pembroke)	154	18 (11.7)	8 (5.2)	26 (16.9)	28	9 (32.1)	7 (25.0)	14 (50.0)	4.6 (0.4)
West Highland White Terrier	138	4 (2.9)	11 (8.0)	15 (10.9)	37	3 (8.1)	7 (18.9)	10 (27.0)	3.3 (0.3)
Whippet	287	3 (1.0)	5 (1.7)	8 (2.8)	47	2 (4.3)	4 (8.5)	6 (12.8)	5.9 (0.3)
Yorkshire Terrier	123	6 (4.9)	5 (4.1)	11 (8.9)	35	5 (14.3)	4 (11.4)	8 (22.9)	3.2 (0.3)
Total	53,537	2265 (4.2)	1973 (3.7)	4238 (7.9)	9937	1521 (15.3)	1325 (13.3)	2452 (26.7)	5.0 (0.0)

ENM, Early neonatal mortality; n_l, number of litters; n_p, number of puppies; PNM, perinatal mortality.

of the litters followed by 47.8% (22/46) in the Dalmatian, 37.9% (11/29) among Great Danes and 37.2% (51/137) in the Bernese Mountain Dog. For the Australian Terrier (0/22), the Italian Greyhound (0/34) and the Basenji (0/22) no stillbirth was present, while the Bichon Havanaise had stillbirth in 2.7% (2/73) of the litters.

Table 3
Breed size and perinatal mortality risk at puppy and litter level in a population of 224 dog breeds.

Breed size	Puppy level				Litter level				
	Puppies n_p	Stillbirth n_p (%)	ENM n_p (%)	PNM n_p (%)	Litters n_l	Stillbirth n_l (%)	ENM n_l (%)	PNM n_l (%)	Mean litter size Day 8 (±SEM)
Miniature	5912	156 (2.6)	194 (3.3)	350 (5.9)	1703	137 (8.0)	155 (9.1)	257 (15.1)	3.3 (0.04)
Small	10,590	376 (3.6)	395 (3.7)	771 (7.3)	2548	285 (11.2)	297 (11.7)	514 (20.2)	3.9 (0.03)
Medium	16,801	641 (3.8)	587 (3.5)	1228 (7.3)	2928	430 (14.7)	404 (13.8)	716 (24.5)	5.3 (0.04)
Large	20,461	1037 (5.1)	754 (3.7)	1791 (8.8)	2974	641 (21.6)	462 (15.5)	926 (31.1)	6.3 (0.05)
Giant	4675	314 (6.7)	230 (4.9)	544 (11.6)	657	174 (26.5)	121 (18.4)	247 (37.6)	6.3 (0.12)
Total	58,439	2524 (4.3)	2160 (3.7)	4684 (8.0)	10,810	1667 (15.4)	1439 (13.3)	2660 (24.6)	5.0 (0.02)

ENM, Early neonatal mortality; n_l, number of litters; n_p, number of puppies; PNM, perinatal mortality.

Dalmatian had the highest risk of litters with early neonatal mortality (43.5%, 20/46) at litter level, followed by Dogue de Bordeaux (38.5%, 10/26), Leonberger (34.8%, 16/46) and Great Dane (31.0%, 9/29). No early neonatal mortality was present among the breeds Basenji (0/22) and Tibetan Terrier (0/28), while Italian Greyhound and Japanese Spitz had a litter risk of early neonatal mortality of 2.9% (1/34) and 3.3% (3/91), respectively.

Also at litter level, variations in the perinatal mortality risk existed between breeds (46) in the Dalmatian, 37.9% (11/29) among Great Danes and 37.2% (51/137) in the Bernese Mountain Dog. For the Australian Terrier (0/22), the Italian Greyhound (0/34) and the Basenji (0/22) no stillbirth was present, while the bichon Havanaise had stillbirth in 2.7% (2/73) of the litters.

Dalmatian had the highest risk of litters with early neonatal mortality (43.5%, 20/46) at litter level, followed by Dogue de Bordeaux (38.5%, 10/26), Leonberger (34.8%, 16/46) and Great Dane (31.0%, 9/29). No early neonatal mortality was present among the breeds Basenji (0/22) and Tibetan Terrier (0/28), while Italian Greyhound and Japanese Spitz had a litter risk of early neonatal mortality of 2.9% (1/34) and 3.3% (3/91), respectively.

Eight days after birth, the highest mean litter size among the 100 most popular breeds was found in the Flat Coated Retriever with 7.6 (± 0.3) puppies, followed by 7.5 (± 0.4) in German Shorthaired Pointer and 7.3 in both the Leonberger and the Rhodesian Ridgeback (± 0.5 and ± 0.4, respectively). The lowest mean litter size at eight days after birth was 2.2 puppies and was found in the Pomeranian, the Toy Poodle and the Norfolk Terrier (± 0.1, ± 0.1 and ± 0.2, respectively). Further information is given in Table 2 and Supplementary File 1.

Table 4
Litter size and perinatal mortality risk at puppy and litter level.

Litter size at birth	Puppy level				Litter level				
	Puppies n_p	Stillbirth n_p (%)	ENM n_p (%)	PNM n_p (%)	Litters n_l	Stillbirth n_l (%)	ENM n_l (%)	PNM n_l (%)	Mean litter size Day 8 (±SEM)
1	533	0 (0.0)	0 (0.0)	0 (0.0)	533	0 (0.0)	0 (0.0)	0 (0.0)	—
2	1744	58 (3.3)	55 (3.2)	113 (6.5)	872	58 (6.7)	55 (6.3)	113 (13.0)	1.9 (0.01)
3	4101	165 (4.0)	141 (3.4)	306 (7.5)	1367	139 (10.2)	123 (9.0)	242 (17.7)	2.8 (0.01)
4	6388	220 (3.4)	219 (3.4)	439 (6.9)	1597	184 (11.5)	182 (11.4)	320 (20.0)	3.7 (0.02)
5	8075	270 (3.3)	250 (3.1)	520 (6.4)	1615	207 (12.8)	189 (11.7)	354 (21.9)	4.7 (0.02)
6	8550	316 (3.7)	314 (3.7)	630 (7.4)	1425	222 (15.6)	209 (14.7)	373 (26.2)	5.6 (0.02)
7	8043	259 (3.2)	222 (2.8)	481 (6.0)	1149	185 (16.1)	153 (13.3)	299 (26.0)	6.6 (0.03)
8	6872	279 (4.1)	252 (3.7)	531 (7.7)	859	176 (20.5)	161 (18.7)	289 (33.6)	7.4 (0.04)
9	5418	257 (4.7)	206 (3.8)	463 (8.5)	602	164 (27.2)	128 (21.3)	235 (39.0)	8.2 (0.05)
10	3770	227 (6.0)	141 (3.7)	368 (9.8)	377	136 (36.1)	85 (22.5)	180 (47.7)	9.0 (0.07)
11	2277	160 (7.0)	141 (6.2)	301 (13.2)	207	80 (38.6)	59 (28.5)	110 (53.1)	9.6 (0.14)
≥12	2668	313 (11.7)	219 (8.2)	532 (19.9)	207	116 (56.0)	95 (45.9)	145 (70.0)	10.3 (0.17)
Total	58,439	2524 (4.3)	2160 (3.7)	4684 (8.0)	10,810	1667 (15.4)	1439 (13.3)	2660 (24.6)	5.0 (0.02)

ENM, Early neonatal mortality; n_l, number of litters; n_p, number of puppies; PNM, perinatal mortality.

Table 5
Age of the bitch and perinatal mortality at puppy and litter level.

Age of bitch (years)	Puppy level				Litter level				
	Puppies n_p	Stillbirth n_p (%)	ENM n_p (%)	PNM n_p (%)	Litters n_l	Stillbirth n_l (%)	ENM n_l (%)	PNM n_l (%)	Mean litter size Day 8 (± SEM)
<1	95	2 (2.1)	6 (6.3)	8 (8.4)	20	1 (5.0)	4 (20.0)	5 (25.0)	4.4 (0.42)
1	4132	158 (3.8)	164 (4.0)	322 (7.8)	879	110 (12.5)	121 (13.8)	202 (23.0)	4.3 (0.07)
2	12,985	476 (3.7)	435 (3.4)	911 (7.1)	2451	331 (13.5)	303 (12.4)	548 (22.4)	4.9 (0.05)
3	12,829	493 (3.8)	430 (3.4)	923 (7.2)	2274	346 (15.2)	273 (12.0)	529 (23.3)	5.2 (0.05)
4	9883	428 (4.3)	343 (3.5)	771 (7.8)	1765	284 (16.1)	238 (13.5)	449 (25.4)	5.2 (0.06)
5	7946	400 (5.0)	301 (3.8)	701 (8.8)	1438	233 (16.2)	187 (13.0)	367 (25.5)	5.0 (0.07)
6	5584	272 (4.9)	239 (4.3)	511 (9.2)	1005	188 (18.7)	164 (16.3)	292 (29.0)	4.8 (0.07)
7	2912	167 (5.7)	132 (4.5)	299 (10.3)	546	102 (18.7)	84 (15.4)	155 (28.4)	4.3 (0.10)
8	1331	94 (7.1)	84 (6.3)	178 (13.4)	268	51 (19.0)	47 (17.5)	80 (29.9)	3.9 (0.14)
9	370	21 (5.7)	20 (5.4)	41 (11.1)	84	11 (13.1)	13 (15.5)	21 (25.0)	3.8 (0.24)
10	85	5 (5.9)	5 (5.9)	10 (11.8)	20	4 (20.0)	4 (20.0)	6 (30.0)	3.0 (0.53)
11	20	1 (5.0)	1 (5.0)	2 (10.0)	6	1 (16.7)	1 (16.7)	1 (16.7)	4.8 (0.52)
Unknown	267	7 (2.6)	0 (0.0)	7 (2.6)	54	5 (9.3)	0 (0.0)	5 (9.3)	5.0 (0.43)
Total	58,439	2524 (4.3)	2160 (3.7)	4684 (8.0)	10,810	1667 (15.4)	1439 (13.3)	2660 (24.6)	5.0 (0.02)

ENM, Early neonatal mortality; n_l, number of litters; n_p, number of puppies; PNM, perinatal mortality.

3.3.2. Breed size

The univariable logistic regression showed an association between breed size and the litter risk of perinatal mortality, including stillbirth and early neonatal mortality ($P < 0.001$) at litter level. The proportion of litters with stillborn puppies increased with breed size from 8.0% in miniature breeds to 26.5% in giant breeds, the proportion of litters with early neonatal mortality increased with breed size from 9.1% in miniature breeds to 18.4% in giant breeds, while the litter risk of perinatal mortality increased with breed size from 15.1% in miniature breeds to 37.6% in the giant breeds. In medium, and particularly in large and giant breeds, litters with stillbirth made the largest contribution to the total perinatal mortality. In miniature and small breeds, early neonatal mortality was slightly more common than stillbirth. An overview of breed size and perinatal mortality risk is given in Table 3.

3.3.3. Litter size

The perinatal mortality risk in litters was unconditionally associated with litter size at birth ($P < 0.001$). The risk of both stillbirth and early neonatal mortality increased with litter size at birth (Table 4).

3.3.4. Age of the bitch and litter number

Increasing age of the bitch was unconditionally associated with a higher risk of stillbirth ($P < 0.001$), early neonatal mortality ($P = 0.001$) and total perinatal mortality ($P < 0.001$) in the litters, respectively. Descriptive statistics are presented in Table 5. Increasing litter number

Table 6
Litter number of the bitch and perinatal mortality risk at puppy and litter level.

Litter number	Puppy level				Litter level				
	Puppies n_p	Stillbirth n_p (%)	ENM n_p (%)	PNM n_p (%)	Litters n_l	Stillbirth n_l (%)	ENM n_l (%)	PNM n_l (%)	Mean litter size Day 8 (± SEM)
1	23,905	1127 (4.7)	916 (3.8)	2043 (8.5)	4217	746 (17.7)	623 (14.8)	1166 (27.6)	5.2 (0.04)
2	18,371	796 (4.3)	634 (3.5)	1430 (7.8)	3399	530 (15.6)	408 (12.0)	808 (23.8)	5.0 (0.04)
3	9674	359 (3.7)	370 (3.8)	729 (7.5)	1862	241 (12.9)	243 (13.1)	419 (22.5)	4.8 (0.06)
4	4346	162 (3.7)	167 (3.8)	329 (7.6)	875	97 (11.1)	114 (13.0)	182 (20.8)	4.6 (0.08)
5	1721	67 (3.9)	60 (3.5)	127 (7.4)	359	43 (12.0)	43 (12.0)	72 (20.1)	4.4 (0.12)
6	320	10 (3.1)	13 (4.1)	23 (7.2)	76	7 (9.2)	8 (10.5)	10 (13.2)	3.9 (0.23)
7	83	3 (3.6)	0 (0.0)	3 (3.6)	19	3 (15.8)	0 (0.0)	3 (15.8)	4.2 (0.44)
8	5	0 (0.0)	0 (0.0)	0 (0.0)	1	0 (0.0)	0 (0.0)	0 (0.0)	5.0 (—)
Unknown	14	0 (0.0)	0 (0.0)	0 (0.0)	2	0 (0.0)	0 (0.0)	0 (0.0)	7.0 (1.00)
Total	58,430	2524 (4.3)	2160 (3.7)	4684 (8.0)	10,810	1667 (15.4)	1439 (13.3)	2660 (24.6)	5.0 (0.02)

ENM, Early neonatal mortality; n_l, number of litters; n_p, number of puppies; PNM, perinatal mortality.

Table 7
Odds ratios from three mixed effects logistic regression models on the occurrence of stillborn puppies, early neonatal mortality (death during the first wk of life) or any perinatal mortality (before Day 8) among 10,756 litters of purebred dogs in Norway during 2006 and 2007. All models have ln (litter size) included as offset and breed (n = 224) as a random effect.

Model	Factor	Odds ratio	SE	P value	95% CI
Stillbirth*	Litter size	1.10	0.01	<0.001	1.07, 1.13
	Bitch age (years)	1.22	0.02	<0.001	1.18, 1.27
	Litter Number†: 1	Baseline†			
	Litter Number: 2	0.75	0.05	<0.001	0.66, 0.86
	Litter Number: 3	0.50	0.05	<0.001	0.42, 0.61
	Litter Number: ≥4	0.38	0.05	<0.001	0.31, 0.49
Early neonatal mortality*	Litter size	1.04	0.01	0.009	1.01, 1.06
	Bitch age (years)	1.08	0.02	<0.001	1.04, 1.12
	First litter	1.26	0.08	0.001	1.10, 1.43
	Stillbirth	2.12	0.15	<0.001	1.84, 2.43
Perinatal mortality*	Litter size	1.09	0.13	<0.001	1.06, 1.11
	Bitch age (years)	1.18	0.02	<0.001	1.14, 1.22
	Litter Number†: 1	Baseline	—	—	—
	Litter Number: 2	0.72	0.04	<0.001	0.64, 0.81
	Litter Number: 3	0.59	0.05	<0.001	0.51, 0.69
	Litter Number: ≥4	0.46	0.04	<0.001	0.38, 0.56
	Size†: miniature	Baseline			
	Size: small	1.09	0.21	0.643	0.75, 1.60
	Size: medium	0.76	0.14	0.134	0.53, 1.09
	Size: large	0.81	0.15	0.253	0.56, 1.17
	Size: giant	1.32	0.32	0.257	0.82, 2.11

* Intraclass correlation coefficient (rho): 0.09 (stillbirth), 0.05 (early neonatal mortality), 0.08 (perinatal mortality)

† Likelihood ratio tests of overall significance of categorical variables: Litter number in stillbirth model P < 0.001. Perinatal model: litter number P < 0.001, breed size group P = 0.018.

was unconditionally associated with a reduced risk of stillbirth (P < 0.001), early neonatal mortality (P = 0.008) and perinatal mortality (P < 0.001) in the litters. Descriptive statistics showed that the highest perinatal mortality risk was found in the first litter of the bitch (Table 6).

3.3.5. Season

Initial unconditional analysis showed that litters born during the fall season had a higher risk of experiencing early neonatal mortality than litters born during spring, summer or winter (data not shown). However, no association between birth season and perinatal mortality, neither stillbirth or early neonatal mortality, was found in the initial multivariable analysis at litter level. Therefore, season was excluded as a parameter in the final multivariable models.

3.3.6. Multivariable analysis

Random effects logistic models were fitted for the three outcomes; stillbirth (0/1), early neonatal mortality (0/1) and any perinatal mortality (0/1) in a litter. The age of the bitch was unknown for 54 of the 10,810 litters, hence 10,756 litters were included in the models. The number of litters in each group (= breed: n = 224) ranged from one to 465 with a mean of 45. The random breed effect was significant in all three models (P < 0.001). After controlling for breed in this manner, breed size group was only significant in the model of total perinatal mortality. The estimated odds ratios (ORs) from the three models are shown in Table 7. In the stillbirth model, a significant interaction existed between the two variables bitch age and litter number (data not shown). A separate model was built where these variables were dichotomized to evaluate the combined effect of the bitch being more than six y old (OR = 1.45) and first litter (OR = 1.27), and the effect of these variables combined gave an estimated OR of 3.00.

A considerable part of the litters with stillbirths also experienced early neonatal mortality. Based upon the model presented in Table 7, it can be seen that the odds of experiencing puppy death during the first wk were doubled (OR = 2.12) among litters with stillborn puppies.

For every one-puppy increase in litter size, the odds of stillbirth increased by 10%, as can be seen by the OR of 1.10 for litter size in the stillbirth model presented in Table 7. Similarly, the odds of puppy death during the first wk and any perinatal mortality increased by 4% and 9%, respectively, per one-puppy increase in litter size.

The estimated intraclass (breed) correlation coefficient (rho) ranged between 0.045 and 0.09, indicating a moderate to low level of within breed clustering, although significant in all three models ($P < 0.001$). In other words, 5% to 9% of the variation in the risk of puppy losses could be explained by the breed, while the remainder of the variation existed at the individual litter level. Model diagnostics revealed no major shortcomings regarding model-fit.

4. Discussion

4.1. Study population

In this cohort study, the risk of stillbirth, early neonatal mortality and total perinatal mortality was estimated for puppies ($n_p = 58,439$) and among litters ($n_l = 10,810$) registered in the NKC during 2006 and 2007. Estimated perinatal mortality in a population of purebred dogs will vary with the breeds that are studied. For 87 of the 224 breeds in this study, nine litters or less were registered in the NKC database and estimates based on these breeds are regarded as less certain. The perinatal mortality risk in our study was 8.0%, with 4.3% stillbirth and 3.7% early neonatal mortality, and this is considerably lower than what is found in other studies. A study from Australia which included 44 breeds with 2574 puppies from 500 litters found 18.5% perinatal mortality, with 7.0% stillbirth and 11.5% early neonatal mortality [4]. In an older study from Great Britain which included 2711 puppies from 111 breeds, the perinatal mortality was 26.3%, with 6.5% stillborn puppies and 19.8% early neonatal morality [5].

A major reason for the low perinatal mortality found in our study is probably that we included far more breeds and litters compared to previous studies. However, underreporting of dead puppies cannot be excluded. Further, data from litters where all puppies died before the time of official registration in the NKC were not reported by the breeders, and therefore not included in the calculations. Most of these litters were probably litters containing a single puppy. Smaller breeds have a lower mean litter size and are more prone to dystocia than larger breeds [17,21]. However, single puppy pregnancies do also occur in larger breeds, and might result in dystocia [21].

A previous study from Norway reported a proportion of stillborn puppies and puppies that died immediately after birth of 7.2% among 265 puppies from 54 bitches with reproduction problems [12] which supports a lower perinatal mortality in purebred dogs in Norway compared to other countries [4,5]. In our study, the total puppy loss from birth to eight wks of age was 9.0%. Close follow-up during gestation, parturition and in the postpartum period are important factors in reducing the perinatal mortality [3] and is probably easier to implement in small-scale dog breeding, like the one practiced in Norway.

Despite of the low perinatal mortality found in the whole study population, for some breeds e.g. the Dogue de Bordeaux, the Dalmatian and the Rhodesian Ridgeback, a high perinatal mortality was detected. In many countries it is common to euthanize puppies with malformations and puppies that don't meet the breed standard. In a study by Gill (2001), congenital defects were found in 2.8% of the puppies. Over 90% of these puppies were born alive and died or were euthanized within 48 h after birth. In addition, 1.7% of the puppies were euthanized because they didn't meet the breed standard [4]. The high early neonatal losses found in some breeds in our study, could possibly be explained by euthanizing of unwanted puppies. But since we don't know if these puppies are reported, the extent of this remains obscure.

Of all puppy losses that occurred from the time of birth to the time of official registration in NKC (approximately eight wks after birth), 89% was caused by perinatal mortality (stillbirths and early neonatal mortality). This supports the findings by Gill (2001) who found that 90.9% of all puppy losses from birth to the six wks after birth were caused by perinatal mortality [4]. It has previously been shown that puppy mortality is highest at birth and within the first days after birth [3,4].

Pathological causes for perinatal mortality in puppies were not examined in this study. The most important causes for perinatal mortality can vary between breeds [4,8]. Fetal asphyxia, where apparently normal puppies are subjected to excessive hypoxia during birth, has previously been identified as one of the main causes of perinatal death [4], in addition to bacterial infections [10]. Post-mortem examinations of 116 puppies that were stillborn or died during the first wk after birth found infections to be the most common cause of perinatal mortality in puppies in Norway by Farstad (1983) [12]. It has also been shown that Fading puppy syndrome is an important cause of early neonatal mortality [3,4].

The OR of mortality in litters was estimated using logistic regression models with litter size as offset. When the frequency of disease (or in this case death) is low, the OR is a good approximation of relative risk and the term risk is therefore used in the discussion of the results [22]. The factors associated with risk of puppy loss during the first wk after birth in the current analyses were breed, breed size (for total perinatal mortality only), litter size, bitch age, litter number and stillbirth (for early neonatal mortality). Each factor will be discussed in more detail below.

4.2. Litter size, breed size and breed

The logistic regression models included litter size as the offset, to account for the fact that the risk of having at least one dead puppy will be higher in larger litters. An additional effect of larger litters, beyond that of having more individuals that could be lost, was detected for the three different outcomes.

The significant relationship between litter size and stillbirth is in line with a study of four large breeds performed by Indrebø et al. (2007). Births of long duration increase the risk of stillborn puppies and weak puppies that die shortly after birth [3,21]. Stillbirth is also often the result of complications during labor which give a higher risk of weak newborn puppies and could explain why the risk of early neonatal mortality was doubled in litters with stillborn puppies. A previous study evaluated the acid-base status in 33 spontaneously born Beagle puppies surviving for more than 48 h. Two h after birth, the base excess in nine puppies with severe respiratory-metabolic acidosis, of which eight were born in a posterior position, was no longer significantly different from the base excess measured in puppies born less acidotic [23]. However, Gill (2001) found that fetal asphyxia was an important cause of stillborn puppies and puppies that were born distressed and subsequently died, most often within 24 h, and concluded that half of these deaths were probably caused by dystocia [4]. Fetal malpresentation, uterine disturbances and prolonged parturition are common causes for dystocia that are found to increase the risk of hypoxic and stillborn puppies [21].

Increasing breed size is associated with increasing litter size [17]. However, our study showed that increasing breed size only remained a significant predictor of total perinatal mortality after factors, such as litter size, bitch age and litter number were controlled for in the multilevel logistic regression models. The increased perinatal mortality in large and giant breeds could be explained by a higher risk of trauma to the puppies caused by the bitch during and after birth and a limited number of teats.

Breed differences in perinatal mortality could partially be explained by anatomical, physiological and genetic features. Dogs have a large diversity in body shape and body size compared to other animal species, and the random effect of breed was significant for all three outcome variables. The smallest breeds had the lowest risk of perinatal mortality, possibly because it is easier for a bitch to take care of a smaller litter. It is well known that the ratio of body weight of the bitch compared to the body weight of the puppies is larger in large and giant breeds compared to miniatures and small breeds. Puppies from smaller breeds could be less vulnerable to trauma caused by the bitch compared to puppies from larger breeds.

The giant, brachycephalic breed Dogue de Bordeaux had the highest perinatal mortality risk among all the breeds studied, which might be explained by its large body, massive head and the high mean litter size at birth of 8.1 puppies [17,24]. In the Purebred Dog Survey conducted in the UK in 2004, 27.8% of the Dogue de Bordeaux litters were born by cesarean section [25]. Uterine inertia is linked with dystocia and it is exaggerated in breeds with heads that are comparatively large for their body size, since more uterine force is needed to expel the puppies [24].

The perinatal mortality in Dalmatians was also among the highest in our study. In the Dalmatian, the mean litter size at birth was 8.4 puppies [17]. Despite of the large puppy loss, the Dalmatian still had a relatively large mean litter size eight days after birth of 6.7 puppies, compared to the mean litter size of 6.3 puppies found in other large breeds. A possible explanation for the relatively high early neonatal risk in this breed could be elective euthanasia of puppies with patches (which is disqualifying at shows) in large litters to reduce litter size.

The early neonatal mortality was also high in the Rhodesian Ridgeback (11.6%), which was the breed with the largest litter size at birth (8.9 puppies) among the 100 most popular breeds [17]. Elective euthanasia because of congenital defects (e.g. dermoid sinus) or because of wrong ridge pattern/lack of ridge in large litters to reduce litter size could possible contribute to the relatively high early neonatal mortality. The frequency of ridgeless offspring has been estimated to 5.6% in the Swedish Rhodesian Rigeback population [26].

In some breeds, like the Boxer, elective euthanasia of puppies with disqualifying coat color is practiced in many countries [4,6]. In a study of 414 Boxer litters with 2629 puppies from the Netherlands, 3.9% of the puppies were euthanized because of white coat color, which is disqualifying at dog shows. The perinatal mortality before eight days of age was 16.8% in the Dutch publication, out of which 5.6% were stillborn [6]. The stillbirth proportion was more than twice as high as the 2.2% found in the current analysis. The mean litter size in Boxers at eight days of age in our study was 6.3, which is 1.0 puppy more than in the study performed by Nielen et al. (1998) (5.3 puppies). The reason for this larger litter size in Boxers in our study might be that a large part of the white puppies are kept in Norway (*personal communication*, the Norwegian Boxer Club), therefore an underreporting of euthanized white Boxers is assumed to be low in the current analysis.

4.3. Age of the bitch and litter number

The risk of having dead puppies increased with increasing age of the bitch in all the three models presented in Table 7.

For overall perinatal mortality, the risk increased by 18% for each 1 y increase in bitch age, while for stillbirth and death during the first wk the risk increased by 22% and 8% per 1 y increase, respectively. Additionally, for stillbirth, there was a significant interaction between age of the bitch and litter number. For ease of interpretation this was evaluated in a separate model as the interaction between the first litter and bitches older than 6 y. These bitches had an increase in the risk of stillbirth beyond what could be expected based on the two predictors alone. Our results support the finding by Münnich et al. (2009) where older primiparous bitches (> 6 y of age) had a significantly higher risk of having special obstetrical conditions and stillbirths compared to young primiparous bitches. Bitches over the age of 6 have more single puppy pregnancies, uterine disorders and prolonged parturitions [21]. Together, this reinforces the recommendation from the NKC not to breed bitches above the age of 6 for the first time. Furthermore, all our three models revealed that the risk of perinatal mortality decreased with increasing litter number suggesting that the more "experienced" mothers might be better care-givers, maybe because breeders choose to breed bitches with good mothering and whelping abilities.

In a study from Australia of 44 breeds, bitches aged one y had the lowest perinatal losses, and with a few exceptions, losses increased with increasing maternal age. However, in the statistical analysis of the litter data for all litters and breed groups, maternal age was not found as a significant predictor of mortality [4]. Beagle bitches were found to have the lowest puppy mortality at 3 y of age, and if the bitch was more than 4–5 y old at the first whelping, the risk of complications was considered elevated [8].

4.4. Season

The initial statistical analysis detected an increased risk of early neonatal mortality in litters born during the fall season. This could be a result of the relatively cold Norwegian climate, but it is unlikely, since most dogs are kept inside. However, association between perinatal mortality risk and season of birth was not found in the initial multivariable analysis (data not shown). A possible explanation for this is the short study period of 2 y. Small differences in perinatal mortality according to birth month or season have been found in long-term studies. Over a 5 y period, Rowlands et al. (1950) observed a somewhat higher neonatal mortality in winter (October–March) than in other seasons (spring or summer). The stillbirth rate was not found to be affected by season [9]. Andersen (1957) also concluded that there was a lack of correlation between puppy losses and seasonal variations [8]. A study from Australia conducted over a 7 y period found a seasonal influence on when the puppies died. Early neonatal deaths in winter (June–August) was the most important contributor, followed closely by late neonatal death in spring (September–November) [4].

4.5. Multivariable analysis

A logistic regression approach was chosen for the analysis, with the outcome being the presence or absence of puppy loss in each litter. Because the risk of losing at least one puppy will be greater in larger litters, the ln (litter size) was included as an offset in the models. The risk of losing puppies was assumed to be affected by the breed of the litter and this lack of independence between litters was accounted for by adding a random effect for breed. Risk factors were evaluated at the breed and litter levels, but individual puppy characteristics were not available for this analysis.

The multivariable analysis showed that breed was a more important determinant of perinatal mortality compared to breed size, because breed size only remained a significant predictor in one of the models after breed was taken into account in the random effect models. However, based on the intraclass correlation coefficient (rho) the amount of variation present at the breed level was only between 5% (for early neonatal mortality) and 9% (for stillbirth). In other words, more than 90% of the variation in perinatal mortality was found at the individual litter level. An evaluation of genetic, common-litter and within-litter effects on preweaning mortality was performed in a Dutch birth cohort of Boxer puppies [27]. The conclusion was that additive genetic factors contributed 14% of the total variation in overall mortality, while common-litter and individual puppy factors explained 17% and 69%, respectively. The current analysis did not include information on risk factors at the individual puppy level. However, the results indicate a similar effect in that most of the variation existed at the lowest level of the hierarchy i.e. at the litter level. The practical implication of this is that interventions to reduce canine perinatal mortality should be focused on improving management and care at the level of the individual litter rather than at the breed level.

5. Conclusions

In conclusion, this large-scale epidemiological study revealed several important findings regarding perinatal mortality in purebred dogs. A low canine perinatal mortality was found in most breeds in Norway. However, in some breeds, a higher perinatal mortality was discovered. Statistical analysis showed that the perinatal mortality in litters was significantly influenced by breed, litter number, litters size and age of the bitch, but not by season. The risk of stillbirth was three times as high in litters from bitches having their first litter after the age of 6 y. Further, the risk of early neonatal mortality was doubled in litters with stillborn puppies. Breed was a more important determinant of perinatal mortality in litters compared to breed size. However, more than 90% of the variation in perinatal mortality was found at the individual litter level. To reduce canine perinatal losses, our results indicate that: 1) bitches should not be bred for the first time when they are older than 6 y, 2) good management at the individual litter level is important, and 3) if stillborn puppies are present in a litter at birth, the live-born puppies require extra close monitoring during the perinatal period.

Appendix. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.theriogenology.2011.12.023.

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