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Quantification of the health-status of the Dutch Labrador retriever population

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ABSTRACT

Health issues in purebred dogs are currently considered one of the biggest problems in companion animal health. The Labrador retriever (LR) is one of the most popular dog breeds. The aim of this study was to quantify LR breed health in comparison with mixed-breed dogs (MB), by using four different data sources: a veterinary practice management system (appr. 35,000 unique individuals LR + MB), data from two animal insurance companies (appr. 15,500 and 4500 individuals respectively), and a histopathological laboratory (appr. 4000 individuals).

After extensive recoding of the data, health parameters utilised to quantify breed health were longevity, frequency of practice visits and insurance expense claims, and diagnostic codes. A Kaplan-Meier univariate and multivariable Cox proportional hazard model were used to evaluate longevity. A negative binomial model was used to analyse the frequency of visits, claims, and diagnostic codes in both sets of insurance data. Logistic regression was used to look into the categorical diagnostic codes in the laboratory data.

The median lifespan of the LR was similar (12 years, practice data) or longer (10 versus 8 years, insurance data) than MB for individuals with a known birth and death date. When including censored individuals, survival time in the LR was comparable to MB individuals up to 10 years of age. Above 10 years of age, the LR lived a similar length as MB with a medium to large body size, but shorter than all MB. The LR visited the veterinary practice more often (risk ratio (RR) 1.2, 95% confidence interval 1.2–1.3), and also showed a higher frequency of insurance expense claims (RR 2.2 (2.1–2.3) and RR 1.2 (1.1–1.3) respectively for the two insurance data sets). The largest difference in organ systems between the LR and MB in insurance claims was related to ears (RR 5.3 (4.8–5.8) and RR 2.6 (2.3–3.1)), followed by airways (RR 2.6 (2.4–2.8)), tendons & muscles (RR 2.4 (2.2–2.6) and RR 1.4 (1.1–1.7)), and joints (RR 1.7 (1.3–2.1)), without a difference in median age at diagnosis. The data from the histopathological laboratory suggested a higher disease burden related to oncology for the LR compared to MB (OR 1.2, 95% CI 1.0–1.3). Oncological diagnoses were made at a younger age in the LR (8.8 versus 9.4 years).

The disease burden was significantly higher for the LR than MB, but these results may suffer from substantial bias such as selection bias towards the database, and different behaviour of LR versus MB owners with regards to veterinary care. In the future, longer term population data can corroborate these results.

1. Introduction

The health of dog breeds has become an important topic in recent years (Collins, Asher et al. 2011). The two types of breed related health issues are inherited diseases and extreme conformation traits, which vary per specific breed (Asher, Diesel et al. 2009; Summers, Diesel et al. 2010).

The Labrador retriever (LR) is one of the most popular dog breeds.

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The Dutch LR breed population consists of phenotypic LR, including pedigreed and non-pedigreed dogs, with the pedigreed LR bred in a closed population. More knowledge on the inherited disease status of the LR is needed to inform dog breeders, policy makers and the public. Reported inherited diseases in the Dutch population include orthopaedic issues such as elbow dysplasia (Lavrijsen, Heuven et al. 2012) and hip dysplasia (Lavrijsen, Leegwater et al. 2014), as well as copper-associated hepatitis (Fieten, Gill et al. 2016). From other populations, oncological problems such as cutaneous mast cell tumours were reported (White, Hohenhaus et al. 2011; Shoop, Marlow et al. 2015; Mochizuki, Motsinger-Reif et al. 2017). Recently, a genetic variant related to mast cell tumours was found in both the LR and the Golden retriever (Biasoli, Compston-Garnett et al. 2019). Soft tissue sarcomas of mesenchymal origin are described in the Dutch population of the Golden retriever (Boerkamp, Teske et al. 2014), which might also share a common genetic predisposition with the LR. A disease-specific search in data from veterinary practice showed only overrepresentation of orthopaedic diagnoses in the Dutch LR population (Meijndert, Fieten et al. 2014; Keijser, Meijndert et al. 2017). A comparative Dutch dog population needs to be defined in order to be able to quantify the health of the LR breed. In earlier studies, mixed-breed dogs (MB) were used as a reference population, representing the genetically most heterogeneous dog population (Keijser, Meijndert et al. 2017). A MB is defined as an individual with a mixed lineage, not belonging to any particular breed, including crossbreeds and mongrels.

Our aim is to quantify the health of the LR population in the Netherlands compared to MB through the use of different sources of data.

2. Material and methods

2.1. Population

The LR population in this study refers to the group of exposed individuals, who are, in effect, exposed to the risk factor of being a phenotypic LR, regardless of pedigree. The MB is considered to be unexposed to this risk factor. Data were provided from four different sources and across different time frames (Table 1).

2.2. Data management per data set

2.2.1. General management

Data recoding and cleaning occurred for all four data sets. Unrealistic values, such as a birth date in the future, were set to “not available”. Variables with a missing percentage of 90–100% were excluded from further analysis. New variables were created based either on direct coding such as lifespan if birth and death date were known, or on proxies such as a cremation event as a proxy for death date. Pedigree was determined by the available chip code, with which the individual should be interpreted as a Dutch pedigree recognised by the Fédération Cynologique International, 2019. Age was recoded in birth cohorts relative to the starting point of the data set to allow adjustment for confounding bias in statistical models. Individuals were grouped in birth cohorts with cut-off points of 1, 5 and 10 years before or after the start date of the respective data sets. Supplemental Fig. 1 shows the change in number of rows per data set during the data management process. Data management was performed in R for statistics (R Core Team (2016) and supplemental Table 3, scripts available from first author).

2.2.2. Veterinary practice management system

Individuals in the veterinary practice data originated from 33 veterinary practices and had a unique identification number within the set. The maximum recorded weight of an individual was selected out of multiple measurements, to limit inclusion of weight during growth. Breed names were highly variable in the original data as the field was free text, resulting in typing errors and alternative spellings. The selection steps of the over 8000 types of entries resulted in three levels of breed: LR, MB, or other specific breeds. The definition of MB was based on the Dutch equivalents of “mongrel”, or a combination of two different breed names. No diagnostic data was available in the practice data, only a date of visit.

2.2.3. Animal insurance companies

Individuals in both insurance data sets had a unique identification number within the set. Breed names were coded at the data source. Breed names available were: LR, MB, other specific breeds and “unknown”. Individuals labelled as breed “unknown” were assumed to be MB for the current analysis.

2.2.4. Histopathological laboratory

Individuals in the pathology data were identified by unique information regarding breed, date of birth, sex, zip code and name. Histopathological examination was available with year and month information. Results of examinations occurring within two months of each other were combined and the first (combined) examination record used for analysis. To enable the calculation of time to event, all examinations were assumed to occur on the 15th of the month. Breed labels were produced from a free text field and recoded. If a specific breed could be deduced from the free text, it was relabelled as such. If the breed was not clear it was labelled as an unknown breed. If it was clearly MB, it was relabelled as MB in the new breed label. Similar relabelling was carried out for the LR.

2.3. Diagnostic code analysis

Codes within both sets of insurance data may refer to general veterinary consultations, diagnostics, organ systems or specific medical conditions. For the analysis, certain diagnostic codes were grouped together (see *supplemental tables 1a and 1b*). In the pathology data, most codes were highly specific diagnoses based on protocolled (histo) pathological processes. In the current study, we analysed the code for any kind of tumour, as well as three sub-diagnoses within those tumours: benign tumour (yes/no), soft tissue tumour (yes/no) and mesenchymal origin (yes/no). An overlap between the sub-diagnoses was possible. Individuals with a known age at the time of the event were selected and the presence of any, and different types of, tumours evaluated.

2.4. Statistical methods

The uncorrected difference in survival time between the LR and MB was visually evaluated using the Kaplan-Meier univariate approach,

Table 1
Main features of data used to compare the health of the Labrador retriever and mixed-breed dog population in the Netherlands.

Data	Full source	Time frame	Breed label
Practice	Practice management system “Idexx Animana”	6 years (2012-2017)	Free text
Insurance1	Animal insurance company “Reaal Dier&Zorg”	11 years (2006-2016)	Coded
Insurance2	Animal insurance company “Petplan”	7 years (2010-2016)	Coded
Pathology	Histopathology laboratory “GD Animal health Deventer”	10 years (2006-2015)	Free text

and the crude and adjusted hazard ratio (HR) was determined in the multivariable Cox proportional hazards model analysis. Individuals without a death date were assumed to be censored at the time of the last observation in the data. The frequency of practice visits and insurance expense claims in respectively the practice and insurance data were analysed in a negative binomial model to account for the large number of low counts in the data. Diagnostic codes related to claims occurring in at least 5% of both the LR and MB in the insurance data were selected for this analysis. Logistic regression was used for categorical outcomes in the pathology data.

The Akaike Information Criteria (AIC)-based backward selection method was used to determine the best fitting models with the lowest AIC for all above models, while confounding was checked (> 10% in parameter estimate (Dohoo et al., 2009). Data analyses were performed in R for statistics (R Core Team (2016) and supplemental Table 3, scripts available from first author).

3. Results

3.1. Baseline characteristics

The overall characteristics are shown in Table 2. The percentage of males and females was close to 50/50 in all data sets. In the practice data, not all individuals were microchipped, while neuter status was known for most individuals.

Evaluation of the median year of birth showed that the LR were born slightly earlier than MB in the practice and insurance1 data cohorts. The year of birth suggested a younger group of the LR in the pathology and insurance2 data (Table 3).

3.2. Results per data set

3.2.1. Practice management system (n LR/MB = 10,429/24,670)

The median lifespan of approximately 12 years was similar for the LR and MB when a birth and death date was available (Table 4). The weight distribution for all individuals for whom a weight was recorded is shown in Fig. 1. The median weight (interquartile range) for the LR was 30.0 kg (25.0–35.1) and for MB 12.4 kg (7.0–23.3).

Survival analysis for all individuals in the data set (including censored individuals) violated the proportional hazard assumption (Fig. 2a). Based on Fig. 2a, it was decided to use two different models up to and above 10 years of age, with the proportional hazard assumption holding for both models. The adjusted (sex and neuter status) HR (CI), based on a Cox model, for individuals up to 10 years of age was 0.8 (0.7-0.9) for the LR compared to MB, indicating a lower death rate for the LR (*see also* supplemental Fig. 2 *for the uncorrected visual illustration*). Above 10 years of age, the adjusted (sex and neuter status) HR (CI), based on a Cox model, for all the LR with a registered weight compared to MB > 25 kg in weight was 1.2 (0.8–1.9), indicating similar death rates (Fig. 2b).

The frequency of practice visits for MB was approximately eight consultations within the eight-year observation period, with an adjusted RR of 1.2 for the LR (Table 5). The frequency of practice visits for the microchipped LR showed a significant difference between pedigreed and non-pedigreed LR versus MB, with an adjusted RR of 1.6 (1.6–1.7)

Table 3
Year of birth distribution with interquartile range (iqr) of the population of Labrador retrievers (LR) and mixed-breed dogs (MB) within a practice management system, two animal insurance companies, and a histopathological laboratory in the Netherlands.

Data source (time frame)	LR median (iqr)	MB median (iqr)
Practice (2012-2017)	2008 (2004-2012)	2009 (2004-2012)
Insurance1 (2006-2016)	2008 (2003-2012)	2009 (2003-2012)
Insurance2 (2010-2016)	2011 (2009-2012)	2010 (2009-2012)
Pathology (2006-2015)	2003 (2000-2005)	2002 (1999-2006)

Table 4
Median lifespan in years and interquartile range (iqr) from two different Dutch data sources for Labrador retrievers (LR) and mixed-breed dogs (MB) for which both birth and death date was recorded.

Data source (time frame)	N LR/MB	Median lifespan in years (iqr)	
		LR	MB
Practice (2012-2017)	1,782/4,009	12.2 (10.4-13.6)	13.0 (10.2-14.8)
Insurance1 (2006-2016)	399/310	10.3 (7.3-12.1)	7.6 (3.3-11.3)

Table 2
Baseline characteristics of the population of Labrador retrievers (LR) and mixed-breed dogs (MB), within data sets from a practice management system, two animal insurance companies, and a histopathological laboratory in the Netherlands.

	Practice (2012-2017)		Insurance1 (2006-2016)		Insurance2 (2010-2016)		Pathology (2006-2015)	
Breed	LR	MB	LR	MB	LR	MB	LR	MB
Total # individuals	10,429	24,670	7151	8412	3156	1389	1,592	2,576
Variable	n (%)[1]	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Sex								
Female	4,947 (47.4)	11,731 (47.6)	3229 (45.1)	4209 (50.0)	1444 (45.8)	714 (51.4)	729 (45.8)	1301 (50.5)
Male	5,094 (48.9)	12,153 (49.3)	3906 (54.6)	4174 (49.6)	1709 (54.2)	672 (48.4)	836 (52.5)	1228 (47.7)
Unknown	388 (3.7)	786 (3.2)	16 (0.2)	29 (0.4)	3 (0.0)	3 (0.2)	27 (1.7)	47 (1.8)
Neuter status			–		–			
Neutered	5,436 (52.1)	13,308 (53.9)					605 (38.0)	1102 (42.8)
Intact	4,605 (44.2)	10,576 (42.9)					157 (9.9)	246 (9.5)
Unknown	388 (3.7)	786 (3.2)					830 (52.1)	1228 (47.7)
Sex + Neuter status[2]			–		–			
Neutered female	3,143 (63.5)	7251 (61.8)					331 (45.4)	603 (46.3)
Neutered male	2,293 (45.0)	6057 (49.8)					274 (32.8)	498 (40.6)
Chip present[3]							–	
Unknown	4174 (40.3)	11,701 (47.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)		
Yes	6,255 (59.7)	12,969 (52.6)	7151 (100.0)	8412 (100.0)	3156 (100.0)	1389 (100.0)		
Dutch pedigree	2,845 (45.5)[4]	0 (0.0)	3408 (47.7)	0 (0.0)	828 (26.2)	0 (0.0)		
No Dutch pedigree	3,410 (54.5)[4]	12,969 (100.0)	3743 (52.3)	8412 (100.0)	2328 (73.8)	1389 (100.0)		

[1] n = number per category, % for total n per breed group.
[2] % of Sex + Neuter status = neuter status per sex.
[3] Chip mandatory for insurance.
[4] % of pedigree presence calculated for individuals with chip.

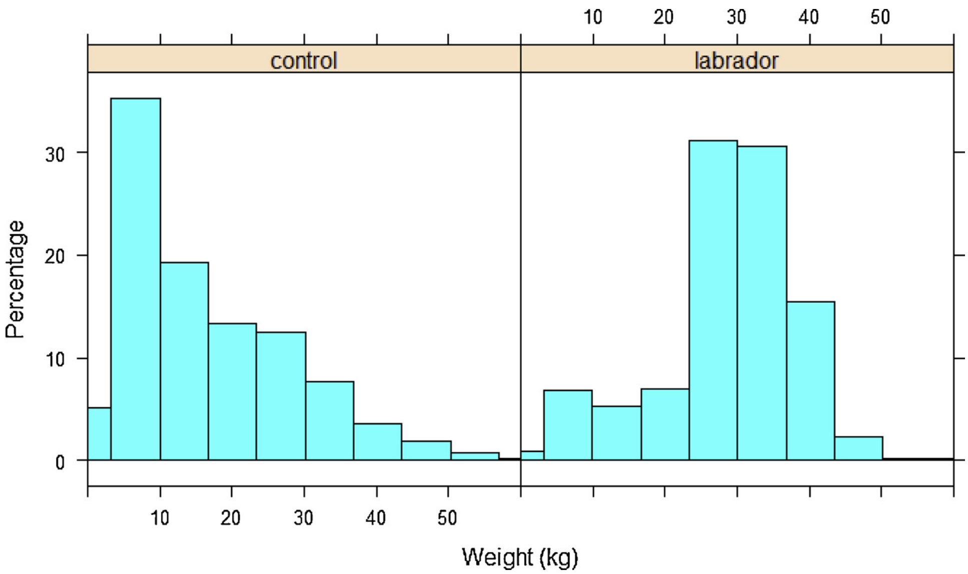

Fig. 1. Maximum recorded weight (kg) distribution of the population of mixed-breed dogs (control, n = 3844 of 24,670) and Labrador retrievers (n = 1478 of 10,429) with a recorded weight within a practice management system in the Netherlands.
Median weight (with interquartile range) was 30.0 kg (25.0–35.1) for Labrador retrievers and 13.0 kg (7.1–24.5) for mixed-breed dogs.

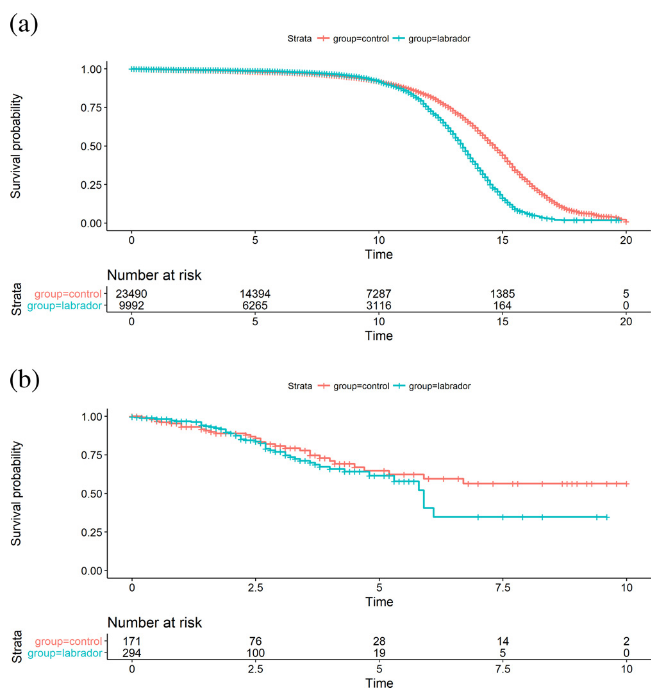

Fig. 2. Survival proportion and time to event in a practice management data set in the Netherlands.
(2a) Survival in years, from birth date to death or censoring event, for all available 9992 Labrador retrievers (labrador) and 23,490 mixed-breed dogs (control). (2b) Survival in years, starting at minimal ten years survival time, from birth date to death or censoring event,for 294 Labrador retrievers with a registered weight (labrador) and 171 mixed-breed dogs > 25 kg in body weight (control). (*See also* supplemental Fig. 2).

and 1.4 (1.3–1.4) respectively.

3.2.2. Animal insurance companies

(insurance1 n LR/MB = 7151/8412; insurance2 n LR/MB = 3156/1389)

The median lifespan of the LR exceeded that of the MB by almost three years for animals with a birth and death date in the insurance1 data (10 versus 7 years, Table 4).

Evaluation of the survival of all individuals in insurance1 showed that the proportional hazard assumption did not hold (Fig. 3a). Based on Fig. 3a, it was decided to use two different models up to and above 10 years of age, with the proportional hazard assumption holding for both models. The adjusted (sex) HR (CI), based on a Cox model, for individuals up to 10 years of age was 0.8 (0.7–1.0) for the LR versus MB (*see also* supplemental Fig. 3 *for the uncorrected visual representation*). The adjusted (sex) HR (CI), based on a Cox model, for LR versus MB with a survival time of at least 10 years was 1.9 (1.5–2.5) (Fig. 3b), showing an increased death rate for the LR.

The frequency of insurance expense claims in the insurance data was defined as an expense claim for any reason. The baseline frequency of claims for the MB in the insurance1 data was 5.1 claims in an 11-year time frame, with an adjusted RR of 2.2 for the LR, indicating twice the rate of insurance claims in the available time frame. In the insurance2 data, the baseline frequency of claims for MB was 5.0 claims in a seven-year time frame, with an RR of 1.2 for the LR (Table 5).

The top three diagnostic codes in the event of an insurance expense claim in the LR compared to MB are ears, tendons & muscles, airways (insurance1), and joints (insurance2) (Table 6). A significant RR > 1 was found for many of the diagnostic codes evaluated (*supplemental* Table 2), with the diagnostic code for ears being the highest (RR = 5.3 (4.8–5.8)). The median age at the first event of the diagnostic code did not differ much between the LR and MB. The crude RR for the top three results in relation to pedigree were also evaluated, often showing a

Table 5
Baseline number of practice visits and insurance expense claims for a mixed-breed dogs (MB) with a Risk Ratio (RR) versus the baseline number of events for Labrador retrievers (LR) in a practice management system, and two animal insurance companies, as analysed with a negative binomial model. CI = 95% confidence interval. Data collected in the Netherlands.

Data source (time frame)	n LR/MB	Baseline number of events MB (CI)	Adjusted RR LR vs. MB (CI)
Practice (2012-2017)	10,429/24,670	8.3 (8.1-8.4)	1.2 (1.2-1.3)[a]
Insurance1 (2006-2016)	7151/8412	5.1 (5.0-5.2)	2.2 (2.1-2.3)
Insurance2 (2010-2016)	3156/1389	5.0 (4.7-5.3)	1.2 (1.1-1.3)

[a] = adjusted for age, sex, neuter status and sex * neuter status, rest adjusted for age.

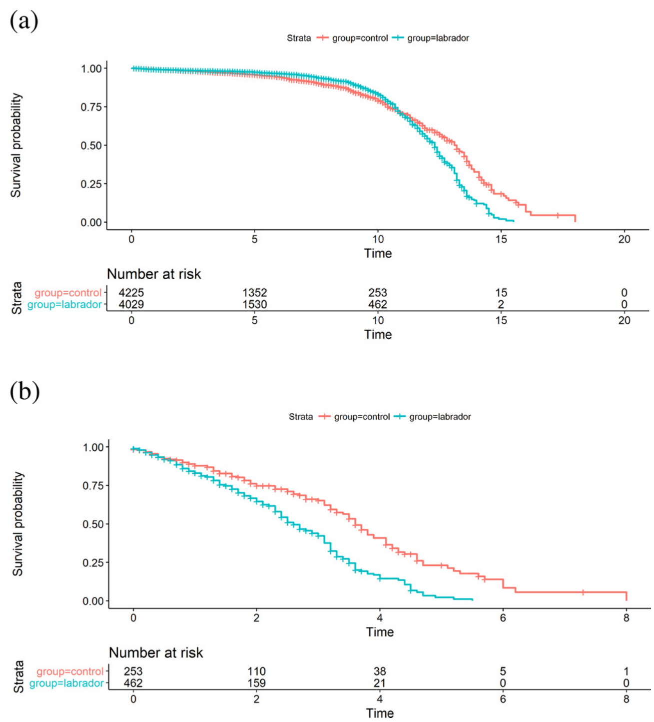

Fig. 3. Survival proportion and time to event in an insurance company data set in the Netherlands.
(3a) Survival in years, from birth date to death or censoring event, for all available 4029 Labrador retrievers (labrador) and 4225 mixed-breed dogs (control). (3b) Survival in years, starting at minimal ten years survival time, from birth date to death or censoring event, for 462 Labrador retrievers (labrador) and 253 mixed-breed dogs (control). (See also supplemental Fig. 3).

significantly higher RR for pedigreed LR than non-pedigreed LR in comparison to MB (Table 6).

3.2.3. Histopathological laboratory (n LR/MB = 1,529/2,576)

The results of the logistic regression model for specific diagnostic tumour codes are shown in Table 7. Tumours originating in mesenchymal cells showed the highest OR (CI) of 1.4 (1.2–1.7) for the LR compared to MB. The median age in years at the first event of the code was consistently lower in the LR than in MB, with the largest difference being 1.1 years.

4. Discussion and conclusion

In this study, the health of the Dutch Labrador retriever (LR) was evaluated by comparing health parameters from four different data sources with that of mixed-breed dogs (MB). We discuss longevity, the number of practice visits and insurance expense claims, as well as specific diagnoses.

4.1. Longevity

The lifespan of approximately 12 years within the practice data was previously found for the LR in the UK (Michell, 1999; O'Neill et al., 2013). The finding of an 11-year lifespan in the LR in the insurance data is closer to what Proschowsky et al. (2003) found earlier in questionnaire data in Denmark. Adams et al. (2016) combined these and other studies to come to a consensus of a 12 year lifespan in general for the LR. McGreevy, Wilson et al. (2018) found a similar lifespan for LR in practice data. Overall, these results suggest similarities between the LR across different subpopulations with regards to lifespan.

The effects of sex and neuter status on longevity, regardless of breed, were as reported earlier (Hoffman et al., 2017; McGreevy,

Table 6
Number of insurance expense claims, with 95% confidence interval (CI) for the top three diagnostic codes in two Dutch animal insurance data sets for the Labrador retriever (LR) compared with the baseline number of expense claims in mixed-breed dogs (MB). Ordered from highest adjusted Risk Ratio (RR) for LR to MB to the lowest, as calculated in a negative binomial model. Diagnostic codes selected for the analysis occurred in at least 5% of both populations. The median age in years with interquartile range (iqr) at first event is shown for individuals with a known age at event. The adjusted RR (CI) for pedigreed and non-pedigreed LR compared to MB are also shown. (See also supplemental Table 2.)

Diagnostic code per data source (time frame)	n cases LR/MB	Baseline number of insurance expense claims (CI) for MB	Adjusted RR (CI) of LR vs MB	Median age, in years at first event (iqr) (n individuals)		Adjusted RR (CI) of LR pedigree and LR no pedigree vs MB
				LR	MB	
Insurance1 (2006-2016)						
Ears	2,518/924	0.2 (0.2-0.2)	5.3 (4.8-5.8)	2.9 (1.2-5.6) (n = 2141)	2.3 (1.1-4.5) (n = 804)	Ped: 6.9 (6.2-7.6) No ped: 3.9 (3.5-4.3)
Airways	2,883/1,859	0.6 (0.5-0.6)	2.6 (2.4-2.8)[a]	2.5 (1.1-5.6) (n = 2236)	2.3 (1.1-4.8) (n = 1495)	Ped: 3.4 (3.1-3.7)[a]No ped: 1.9 (1.7-2.1)[a]
Tendons & Muscles	1,838/1,113	0.3 (0.3-0.3)	2.4 (2.2-2.6)	4.3 (1.2-8.3) (n = 1167)	2.7 (1.1-6.2) (n = 701)	Ped: 2.8 (2.5-3.1) No ped: 2.0 (1.8-2.3)
Insurance2 (2010-2016)						
Ears	982/228	0.3 (0.2-0.3)	2.6 (2.3-3.1)	2.4 (1.3-4.2) (n = 982)	2.3 (1.3-4.0) (n = 228)	Ped: 3.7 (3.1-4.6) No ped: 2.3 (1.9-2.7)
Joints	455/143	0.2 (0.2-0.3)	1.7 (1.3-2.1)	3.0 (1.2-5.6) (n = 454)	3.8 (1.5-6.6) (n = 143)	Ped: 2.1 (1.6-2.9) No ped: 1.5 (1.2-2.0)
Tendons & Muscles	272/99	0.1 (0.1-0.1)	1.4 (1.1-1.7)	3.2 (1.6-5.6) (n = 272)	3.0 (1.9-5.7) (n = 99)	Ped: 1.9 (1.4-2.5) No ped: 1.2 (0.9-1.5)

[a] = adjusted for age and sex, rest is adjusted for age.

Table 7
Adjusted Odds Ratios (OR) with 95% confidence interval (CI) of 4 logistic regression models on diagnostic tumour codes in data from a Dutch histopathological laboratory on biopsies or full animals (2006–2015), for 1505 Labrador retriever (LR) versus 2503 mixed-breed dogs (MB), with median age (interquartile range (iqr)) at diagnosis.

Diagnostic code outcome[1]	n (% of larger total)		Adjusted OR LR vs. MB (CI)	Median age, in years at diagnosis (iqr)	
	LR	MB		LR	MB
Total n	1505	2503		1505	2503
Any tumour	959 (63.7)	1512 (60.4)	1.2 (1.0-1.3)[a]	8.8 (6.8-10.2)	9.4 (7.0-11.5)
Within any tumour: yes					
Benign: yes	453 (47.2)	685 (45.3)	1.1 (0.9-1.3)[a]	8.3 (6.4-9.8)	8.7 (5.7-10.8)
Soft tissue: yes	153 (10.2)	290 (11.6)	0.8 (0.6-1.0)	9.3 (7.7-10.5)	10.4 (8.2-12.0)
Mesenchymal cell origin: yes	382 (25.4)	480 (31.7)	1.4 (1.2-1.7)[a]	8.8 (7.3-10.0)	9.9 (7.8-11.7)

[1] = yes versus no of diagnosis.
[a] = adjusted for age.

Wilson et al. 2018), with females living longer, and intact dogs living shorter than neutered dogs. The Kaplan-Meier plot suggested a change in HR for the LR compared to MB from approximately 10 years of age, with equal death rates for the LR and MB below 10 years of age. The difference in death rate above 10 years of age may be confounded by body size (Michell, 1999; Galis, Van der Sluijs et al. 2007; Adams, Evans et al. 2010), as the median weight of the MB group was less than half that of the LR. The comparison in a Cox model between the LR with a registered weight and MB with a body weight of > 25 kg, showed no significant difference in death rate between LR and MB. We assumed the adult LR to have a body weight of around 30–35 kg (Dutch kennel club (Raad Van Beheer et al., 2019)), while MB with a body weight of > 25 kg excluded smaller dogs with a subsequent longer lifespan. Based on these combined results, we concluded that the LR live shorter than all MB, but similarly long compared to middle and large sized MB. However, longevity in itself is not necessarily a measure of good health because it does not indicate the health and wellbeing during life (O'neill et al., 2017; Keijser et al., 2017).

4.2. Frequency of practice visits and insurance expense claims

The frequency of practice visits in the timeframe available was 20% higher for the LR compared to MB, but the frequency of expense claims was twice as high for the LR compared to MB. Repeated visits or claims could be associated to a single disease episode, thereby overestimating the disease burden. However, this was equally overestimated for the LR and MB, and each practice visit can be seen as a burden for the dog and the owner. It may be that different types of owners visit the veterinary practice sooner and more frequently, and more vet visits lead to more insurance events and a higher likelihood of showing up in pathology data due to samples being further diagnosed. The difference in expense claims between the LR and MB is higher than expected based on visits to primary practice, and could be the result of more claims for medication and preventive medicine in the LR (supplemental Table 2). The possible influence of selection bias is discussed below.

4.3. Diagnostic codes

The RR for specific diagnostic codes also showed a higher insurance expense claim rate in the LR for almost all codes. The most commonly occurring code was general consultation. The top four overrepresented diagnostic codes in the LR were ears, tendons & muscles, joints and airways. Apart from airways, these results are supported by previous studies in the Dutch LR population (Keijser, Meijndert et al. 2017; Keijser, Vernooij et al. 2018), as well as in the UK LR population (McGreevy, Wilson et al. 2018).

The OR for the occurrence of any tumour diagnosis in the pathology data was 1.2,suggesting a higher oncological disease burden for the LR compared to MB. Within tumours, the mesenchymal cell origin had the highest OR, suggesting higher genetic burden for these type of tumours, as was found in the Golden retriever (Boerkamp, Teske et al. 2014). Also, the lower median age at tumour diagnosis in the LR may represent a younger age at the start of the disease. Furthermore, the higher frequency of practice visits by the owners of an LR may account for a faster diagnosis, indicating a potential for detection bias.

The ratio of the LR compared to MB in the pathology data (3 to 5) is skewed towards more LR relative to the source population in the primary practice (2 to 5), leading to an underestimation of the increased tumour risk in the LR. The diagnostic code analyses identified previously unreported health issues such as ear and airway problems in the LR. The results also support the previously reported increased disease burden in the locomotor system, as well as a higher tumour risk for the LR. The potential biases influencing the diagnostic code results is discussed below.

4.4. Pedigree

Pedigree might be associated with decreased health, because the smaller the effective population size, the more likely the spread of deleterious changes in the genes (Marsden, Ortega-Del Vecchyo et al. 2016). Our results suggested no association between pedigree and longevity in the LR (results not shown). However, the frequency of practice visits and insurance expense claims were significantly higher for the pedigreed LR than the non-pedigreed LR. Whether this indicates an increased disease burden in the pedigreed LR or merely suggests a more health conscious or worried owner remains to be elucidated. Also, the pedigree status was unknown for part of the individuals in the data sets, resulting in bias, and - as pedigree is associated with cost - the financial means of the owner of a pedigreed dog versus a non-pedigreed dog may differ.

4.5. Data validity

The data sources explored in this study are a non-random sample of the total dog population, resulting in potential for selection bias. The obvious reasons are that not all owners visit a veterinarian, that in the Netherlands only a limited number of dogs are insured (estimates are < 10%). Also, in daily veterinary practice, even if there is an indication, biopsies are not always taken and examined nor is an autopsy always performed. Even more selection bias may be caused by the veterinarian's laboratory preference, the owner's financial means, and the owner's perception of the choices relating to the health and burden on the animal or themselves, all influencing whether or not a certain diagnostic or treatment procedure is started. There may even be a systematic difference between LR and MB owners. More knowledge about dog owner motivation to own a specific type of dog, such as pedigreed versus non pedigreed or MB, would be interesting.

We consider the practice data to be the best representation of the source population in the Netherlands, because there is only one step between the dog's health and it being present in the data. Other efforts to collect health data from primary practice are available in other countries (O'Neill, 2013; Kass, Weng et al. 2016). The ratio of the LR and MB is skewed towards the LR in the insurance and pathology data, indicating a large risk of selection bias in such data sources, as reviewed earlier (O'Neill et al., 2014).

Information bias was probably present in all data sets, in particular regarding exposure, i.e. breed. It is possible that individuals registered as MB were in fact crossbred dogs or even purebred dogs, reducing the aspired genetic heterogeneity of the reference population. If this is the case, it would reduce the estimated negative effect on health of being an LR in this study. However, it was difficult to ascertain MB status in the available data sources. The outcome variable may also be prone to information bias, but we assume this error to be the same in the LR and MB and thus not influencing the associations.

No confounding was found in the current study for the limited number of available variables. Other external factors such as living circumstances, husbandry and exercise were not available, but may influence health (Adams, Watson et al. 2016; Adams, Ceccarelli et al. 2018).

4.6. Conclusions

The LR live equally long as MB of a similar body size, but shorter than MB of all sizes. In their lives, LR owners visit a veterinary practice and submit a claim to an insurance company more often. Specific diagnoses are related in particular to ear and locomotion problems, while tumours found in the LR were sent to a pathological laboratory more often. All these aspects point to an increased disease burden for the LR, but might be heavily influenced by owner behaviour and financial means. More intensive and improved data collection from veterinary practices, including diagnosis, are needed to conduct further research in the future.

E. van Garderen and P. van Rooijen are employees of the companies that provided the data (see affiliations). The aforementioned authors played no role in the original study design nor in the decision to use these data sources for this study.

Declaration of Competing Interest

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.prevetmed.2019.104764.

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