J. Comp. Path. 2016, Vol. 154, 195–210

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NEOPLASTIC DISEASE

Swiss Feline Cancer Registry 1965–2008: the Influence of Sex, Breed and Age on Tumour Types and Tumour Locations

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Summary

Cancer registries are valuable sources for epidemiological research investigating risk factors underlying different types of cancer incidence. The present study is based on the Swiss Feline Cancer Registry that comprises 51,322 feline patient records, compiled between 1965 and 2008. In these records, 18,375 tumours were reported. The study analyses the influence of sex, neutering status, breed, time and age on the development of the most common tumour types and on their locations, using a multiple logistic regression model. The largest differences between breeds were found in the development of fibrosarcomas and squamous cell carcinomas, as well as in the development of tumours in the skin/subcutis and mammary gland. Differences, although often small, in sex and neutering status were observed in most analyses. Tumours were more frequent in middle-aged and older cats. The sample size allowed detailed analyses of the influence of sex, neutering status, breed and age. Results of the study are mainly consistent with previous analyses; however, some results cannot be compared with the existing literature. Further investigations are necessary, since feline tumours have not been investigated in depth to date. More accurate comparisons would require the definition of international standards for animal cancer registries.

Keywords: cancer registry; cat; statistical analysis; tumour

Introduction

Cancer registries are important tools for establishing cancer control and prevention strategies. They are used in epidemiological research to examine risk factors underlying the incidence of different types of cancer. Tumour initiation and progression are influenced by several factors whose precise interactions are still unknown.

Demographic variables such as sex, age (Parkin, 2006) and breed (Dorn *et al.*, 1968b; Thrusfield, 2007) are typically used to analyse the development of specific cancers.

Companion animals with spontaneously developing tumours are, moreover, valuable resources for investigating the complexity of human cancer pathogenesis, progression and therapy. Pets and people share the same environment and are therefore exposed to similar risk factors. Furthermore, their tumours undergo analogous genetic and molecular alterations and they display similar levels of tumour

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0021-9975/$ - see front matter
http://dx.doi.org/10.1016/j.jcpa.2016.01.008

heterogeneity, which results in similar mechanisms of cancer development, resistance to therapy, recurrence and metastasis (Dorn *et al.*, 1968a; Thrusfield, 1988; MacEwen, 1990; Paoloni and Khanna, 2008). Finally, in-depth examination of animal tumours could lead to the identification of new genes associated with cancer, relevant environmental risk factors and the development of new prognostic, diagnostic and therapeutic applications (Vail and MacEwen, 2000).

The present study is based on analysis of the Swiss Feline Cancer Registry, which consists of 51,322 feline patient records compiled between 1965 and 2008 (Graf *et al.*, 2015). In this extended examination of data from the registry, we analyse the influence of sex, neutering status, breed and age on the development of the most common feline tumour types (i.e. adenoma/adenocarcinoma, fibrosarcoma, lymphoma and squamous cell carcinoma) and tumour locations (i.e. skin and subcutis, mammary gland, gastrointestinal tract, cardiorespiratory system and oral cavity/pharynx), their distribution and relative frequency over the period of study.

Materials and Methods

Data from the Swiss Feline Cancer Registry (Graf *et al.*, 2015) were used for extended analysis. Three veterinary diagnostic laboratories in Switzerland provided the case records.

Feline breeds with at least 90 individual records were investigated further; the remaining breeds were classified as 'other breeds'. The sex of the animals was grouped as following: male, neutered male, female, neutered female and unknown.

To unify the classification of some of the anatomical locations, we changed two specifications: leucosis with the location 'bone marrow' was changed to the location 'unknown' and fibrosarcomas with the location 'skin' were changed to the location 'soft tissue' (subcutis).

Since there is no obligatory registration of cats in Switzerland, there are only approximate estimates of the size of the feline population. Therefore, proportional calculations from the available patient datasets are given.

Data, wherever applicable, were analysed in two groups. In the first group all tumours (i.e. benign and malignant together) were analysed and in the second group only malignant tumours were included.

Using ICD-0-3 for human patients (WHO, 2013), tumour names were sometimes slightly different from those used in veterinary pathology (i.e. malignant lymphoma, mast cell sarcoma and fibromatous neoplasia). 'Basal cell tumour' is also an old term, which is now usually replaced with the terms 'trichoblastoma' or 'sweat gland ductular adenoma'.

Data editing and statistical analyses were performed using Stata Software (StataCorp, 2011; Stata Statistical Software: Release 12; StataCorp, College Station, Texas, USA). Statistical analyses were carried out using Chi-square/Fisher's exact test. Significant variables were further integrated and analysed in a multiple logistic regression model (using binary logistic models and stepwise backward procedure). The following variables were included in the final model as fixed terms: canton of origin, age, sex/neutering status, breed, year and method of examination. $P \leq 0.05$ was considered to be significant and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. The power was set at >0.8.

Results

The Swiss Feline Cancer Registry consists of the records of 51,322 cats that underwent pathological examination. The number of patients with confirmed tumours was 17,856 (34.79%). Some cats were diagnosed with multiple primary tumours, adding up to a total of 18,375 diagnosed tumours. Of these diagnoses, 14,759 (80.32%) tumours were malignant.

Most cats were of the European shorthair breed. In the statistical evaluation, this breed was used as the standard for comparisons with the remaining breeds.

Breed, sex and age distribution of the entire dataset are presented in Graf *et al.* (2015).

The following results introduce the most common tumour types and anatomical locations in cats, the influence of age, breed and sex, as well as occurrence over the years.

Adenoma/Adenocarcinoma

Adenoma/adenocarcinoma was the most common tumour diagnosed between 1965 and 2008. Among the 18,375 diagnosed tumours, 3,515 (19.1%) were either an adenoma or an adenocarcinoma. Of the total number, 2,613 (74.3%) were malignant (adenocarcinomas). In the 1960s, approximately half of the diagnosed tumours were adenomas/adenocarcinomas. Their relative frequency decreased over the period covered by this study (Fig. 1).

The most common anatomical locations of adenoma/adenocarcinoma and adenocarcinoma were the mammary gland, gastrointestinal tract and cardiorespiratory tract (Fig. 2).

Using multiple logistic regression analysis, the odds of cat breeds developing an adenoma/adenocarcinoma were compared with those of the European shorthair cat (OR = 1). Two analyses were carried

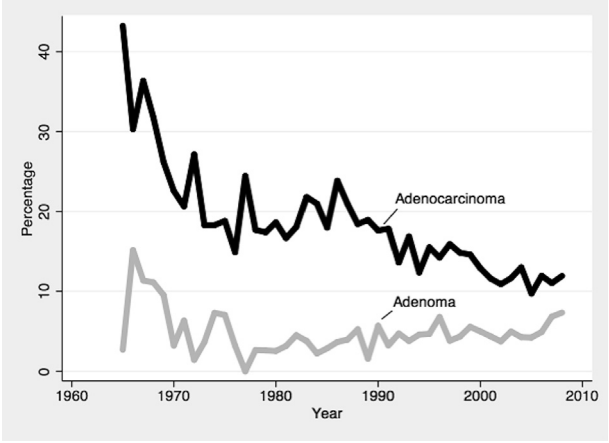

Fig. 1. Relative diagnosis frequency of adenoma ($n = 902$) and adenocarcinoma ($n = 2,613$) expressed as a percentage of the overall tumour diagnoses ($n = 18,375$) between 1965 and 2008.

out, one using the group adenoma/adenocarcinoma (benign and malignant) and one using only adenocarcinomas (malignant) (Fig. 3). In both analyses, only a few breeds had higher odd ratios in comparison with European shorthair cats. Siamese cats (OR = 2.44 [2.07, 2.89]) and Oriental shorthair cats (OR = 2.86 [1.45, 5.61]) had the highest odds ratios when frequency of adenocarcinoma was calculated (see Supplementary data).

Analyses of the influence of age revealed that the odds of cats developing an adenoma/adenocarcinoma or adenocarcinoma increased with age. The odds of a neutered male cat developing an adenoma/adenocarcinoma or adenocarcinoma were significantly higher compared with entire male cats. There was no significant difference between neutered and entire female cats. The odds of a female cat developing an adenoma/adenocarcinoma or adenocarcinoma compared with those of a male cat were significantly higher (Table 1).

Fibroma/Fibrosarcoma

Of 18,375 diagnosed tumours, 3,386 (18.4%) were either a fibroma or a fibrosarcoma. Of these, 3,209 (94.8%) were malignant. Fibroma/fibrosarcoma was a rare diagnosis in the 1960s, but its relative frequency has increased since. This is especially true starting from the 1990s, where fibroma/fibrosarcoma occurrences increased substantially (Fig. 4).

Because fibromas were rare and have no important effect on the analyses, further investigations focused on fibrosarcomas only. The most common anatomical locations for fibrosarcoma were the connective tissues, including subcutis (skin) with 88.5%, followed by unknown location (5.7%) and oral cavity/pharynx (3.1%).

No breed had significantly higher odds of developing a fibrosarcoma compared with the European shorthair cat (OR = 1). However, several breeds had odds ratios that were significantly lower (Fig. 5) (see Supplementary data).

Analyses of the influence of age revealed that fibrosarcomas occurred more frequently in middle-aged and older cats. Neutered and entire male cats had the same odds of developing a fibrosarcoma. Neutered female cats had significantly higher odds than entire female cats. The odds of a female cat developing a fibrosarcoma compared with those of a male cat were significantly higher (Table 1).

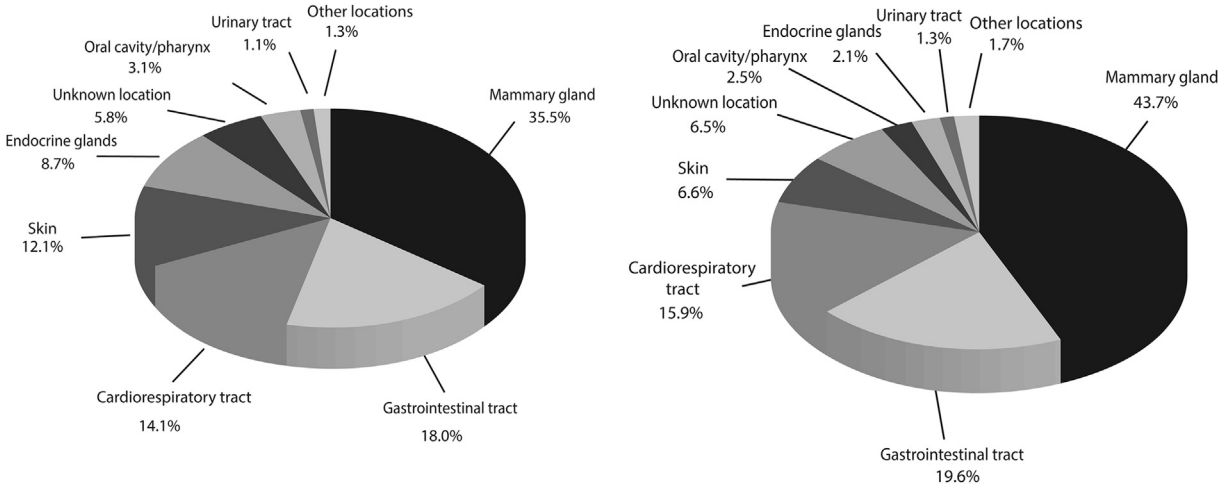

Fig. 2. Most common anatomical locations of adenoma/adenocarcinoma ($n = 3,515$; left) and adenocarcinoma ($n = 2,613$; right).

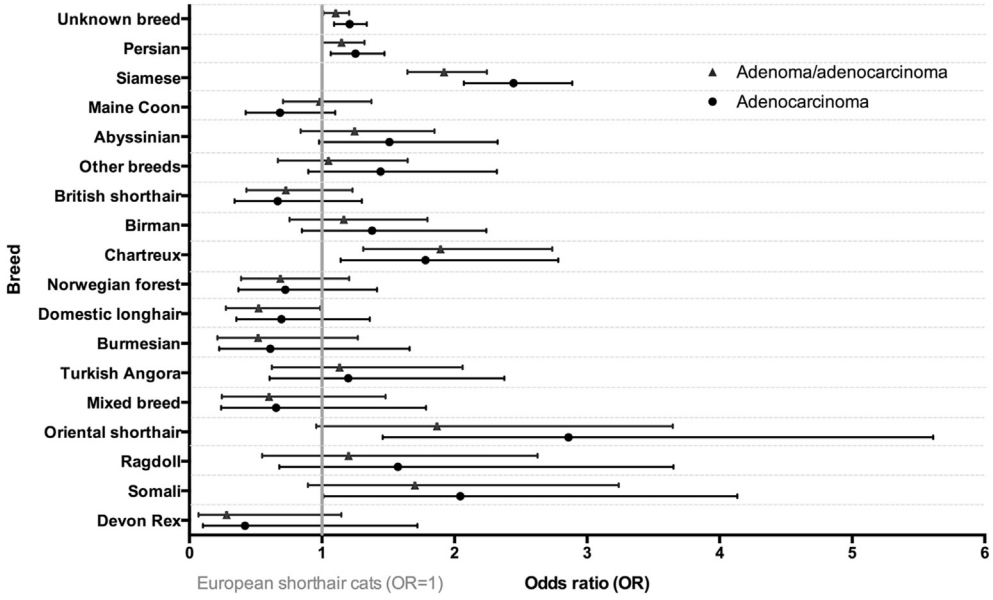

Fig. 3. Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common breeds that develop adenoma/adenocarcinoma (benign and malignant, $n = 3{,}515$) or adenocarcinoma (malignant, $n = 2{,}613$) compared with the European shorthair cat (OR = 1).

Table 1
Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common tumour types comparing sex and neutering status

Tumour type	*Male neutered versus male entire (OR = 1)*		*Female neutered versus female entire (OR = 1)*		*Female versus male (OR = 1)*	
	OR (95% CI)	P	*OR (95% CI)*	*P*	*OR (95% CI)*	P
Adenoma/ adenocarcinoma	1.53 (1.34, 1.75)	0.00	0.95 (0.87, 1.05)	0.31	2.15 (2.00, 2.31)	0.00
Adenocarcinoma	1.53 (1.30, 1.80)	0.00	0.99 (0.89, 1.10)	0.83	2.62 (2.40, 2.87)	0.00
Fibrosarcoma	1.01 (0.90, 1.14)	0.83	1.26 (1.13, 1.41)	0.00	1.12 (1.04, 1.21)	0.00
Lymphoma	1.37 (1.22, 1.54)	0.00	1.49 (1.31, 1.68)	0.00	0.88 (0.81, 0.95)	0.00
Squamous cell carcinoma	1.32 (1.13, 1.54)	0.00	1.30 (1.12, 1.5)	0.00	1.01 (0.92, 1.11)	0.19

Lymphoma

Of 18,375 diagnosed tumours, 2,868 (15.6%) were classified as lymphoma. This tumour type was relatively frequent from 1972 to 1994, where up to 38% of tumour diagnoses were of this type. In the mid-1990s the frequency of lymphoma dropped substantially and the relative frequencies have remained between 10% and 15% since (Fig. 6).

The most common anatomical locations for lymphoma were unknown location, gastrointestinal tract and lymph node (Fig. 7).

Oriental shorthair and Somali cats had significantly higher odd ratios for developing lymphomas compared with those of European shorthair cats. Persian, Maine Coon, British and Norwegian forest cats had significantly lower odds ratios (Fig. 8) (see Supplementary data).

Analyses of the influence of age revealed that the mean age of a cat developing lymphoma was 8.5 years. Lymphomas appeared in all age categories, but were the most frequent tumour type in young cats (<5 years) compared with other tumour types. The odds of a neutered cat developing lymphoma were significantly higher than for entire cats, for both males and females. The odds of a female cat developing lymphoma compared with those of a male cat were significantly lower (Table 1).

Squamous Cell Carcinoma

Of 18,375 diagnosed tumours, 1,811 (9.9%) were squamous cell carcinomas. The frequency of squamous cell carcinomas constantly decreased between the 1960s and the early 1990s and then increased again (Fig. 9).

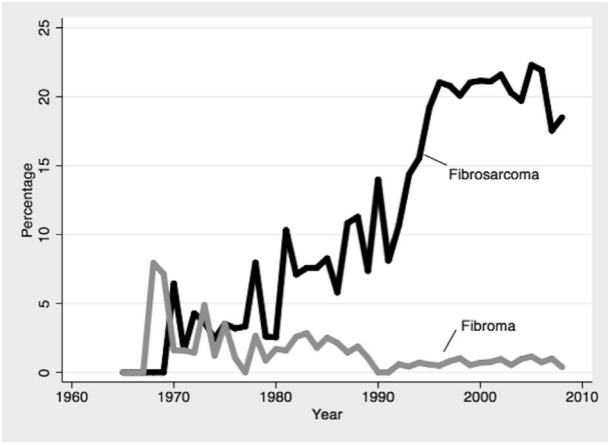

Fig. 4. Relative diagnosis frequency of fibroma ($n = 177$) and fibrosarcoma ($n = 3,209$) expressed as a percentage of the overall tumour diagnoses ($n = 18,375$) during the years 1965–2008.

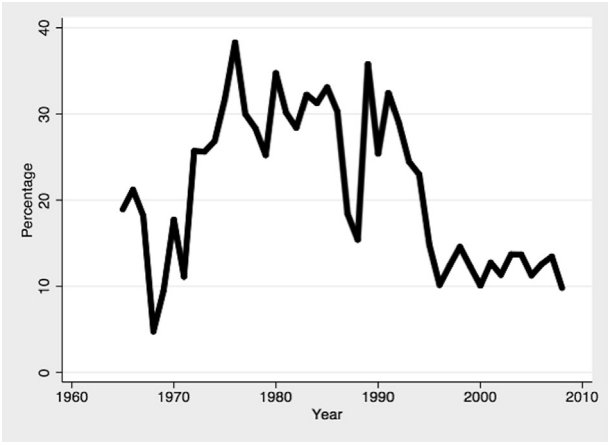

Fig. 6. Relative diagnosis frequency for lymphoma ($n = 2,868$) expressed as a percentage of overall tumour diagnoses ($n = 18,375$) between 1965 and 2008.

The most common anatomical locations for squamous cell carcinomas were the skin (49.3%), followed by the oral cavity/pharynx (29%) and unknown location (9.7%). No other breed had significantly higher odds of developing a squamous cell carcinoma than the European shorthair cat (OR = 1). However, several breeds had significantly lower odds ratios (Fig. 10) (see Supplementary data).

Analyses of the influence of age revealed that the odds of developing a squamous cell carcinoma increased with age, with a mean age at diagnosis of 12.2 years. The odds of a neutered cat developing a squamous cell carcinoma were significantly higher compared with entire cats, for both males and females. There was no significant difference between the odds for female and male cats (Table 1).

Skin and Subcutis

Skin and subcutis were the most common anatomical locations for tumours between 1965 and 2008. Of 18,375 diagnosed tumours, 7,629 (41.5%) were located in the skin and subcutis. Of these, 5,804 (76.1%) were malignant. Benign skin and subcutaneous tumours had a frequency of around 10% between

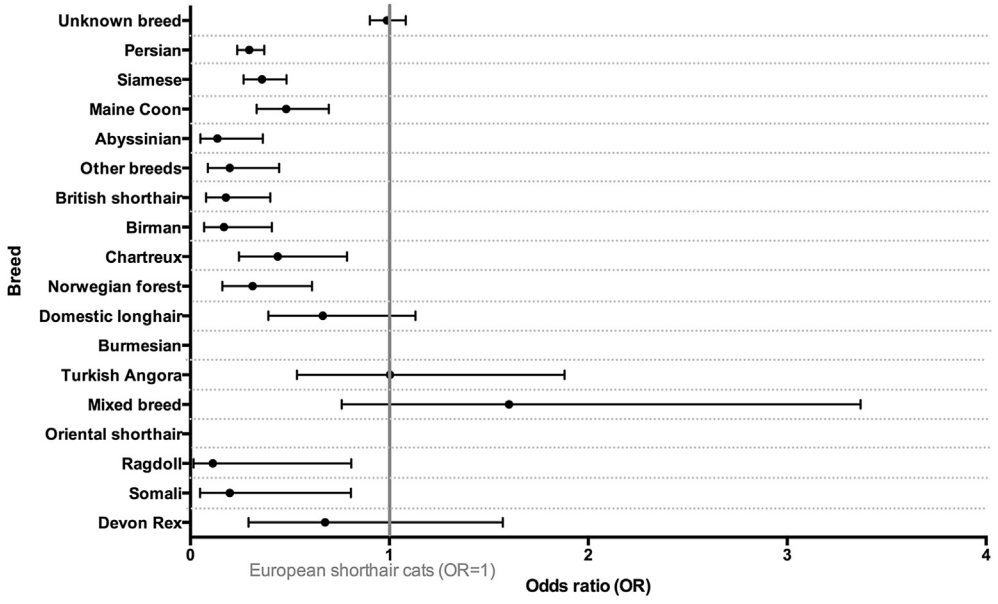

Fig. 5. Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common breeds that develop fibrosarcoma ($n = 3,209$) compared with the European shorthair cat (OR = 1).

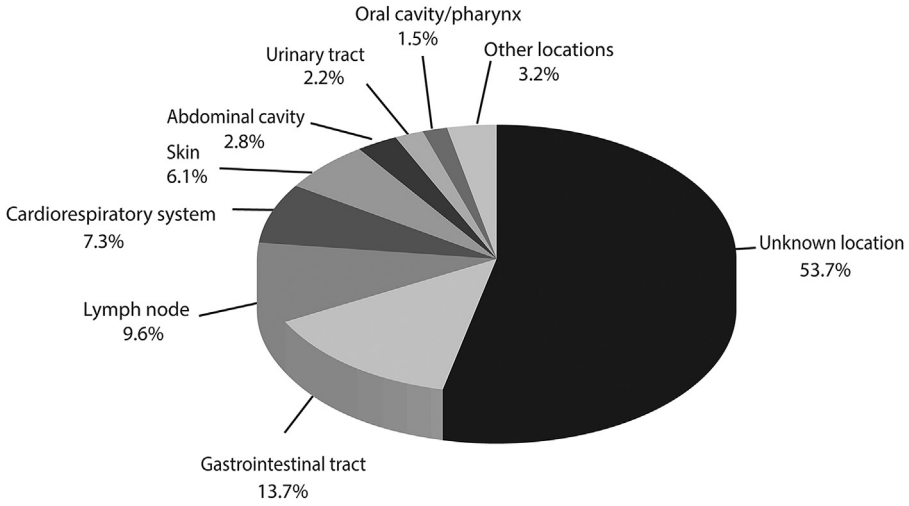

Fig. 7. Occurrences of the most common anatomical locations for lymphoma ($n = 2{,}868$).

1965 and 2008. Malignant tumours increased in the 1990s from around 20% to almost 40% of the overall tumour findings (Fig. 11).

The most common tumour types affecting the skin and subcutis were fibrosarcoma, basal cell tumours and squamous cell carcinoma (Fig. 12).

The European shorthair cat (OR = 1) had the highest odds of developing a tumour in the skin/subcutis; several breeds had significantly lower odds ratios (Fig. 13). In the evaluation of the skin without the subcutis ($n = 4{,}970$), similar results were seen (see Supplementary data).

Analyses of the influence of age revealed that the odds of a cat developing a tumour or a malignant tumour of the skin or subcutis increased with age, with a mean age at diagnosis of 10.5 years. Increasing odds with age were also found for the location skin (without subcutis), with a mean of 10.8 years. Differences in sex/neutering status for developing a tumour of the skin skin/subcutis or skin were small (Table 2).

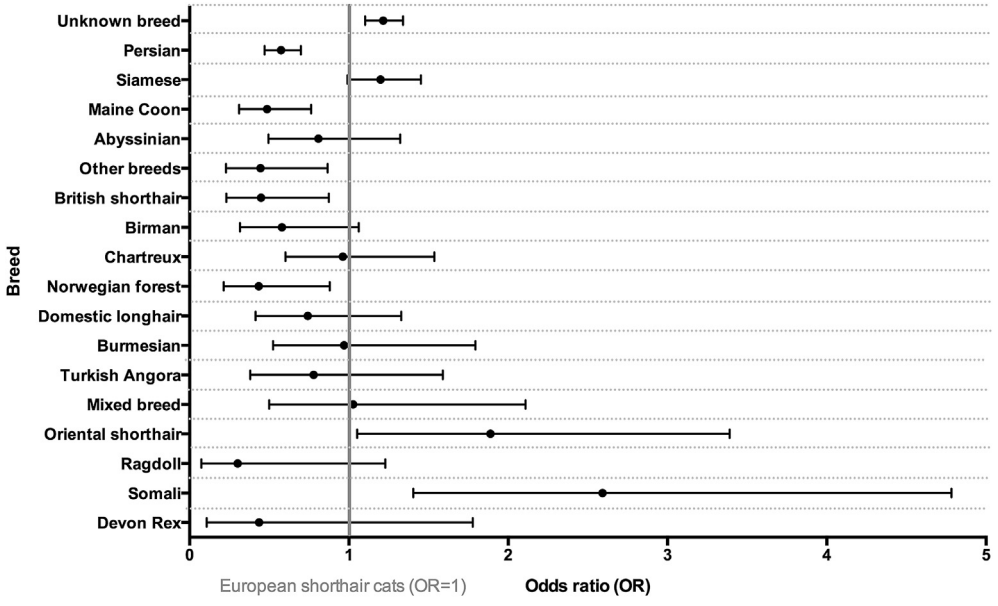

Fig. 8. Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common breeds that develop lymphoma ($n = 2{,}868$) compared with the European shorthair cat (OR = 1).

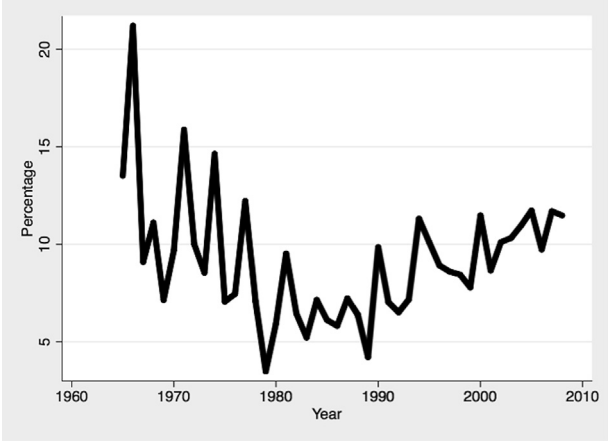

Fig. 9. Relative diagnosis frequency of squamous cell carcinoma ($n = 1{,}811$) expressed as a percentage of overall tumour diagnoses ($n = 18{,}375$) during the years 1965–2008.

Mammary Gland

Of 18,375 diagnosed tumours, 1,501 (8.2%) were in the anatomical location of the mammary gland. Of these, 1,249 (83%) were malignant. The frequency of mammary gland tumours compared with overall tumour findings did not change substantially from 1965 to 2008 (Fig. 14).

The most common mammary tumour types were adenoma/adenocarcinoma (83.08%), fibromatous neoplasia (3.8%) and epithelial neoplasia not otherwise specified (NOS) (3.6%). Adenocarcinoma (91.4%) and epithelial neoplasia NOS (2.4%) were found most often when comparing malignant tumours only.

No breed had significantly lower odds of developing a mammary tumour/malignant tumour than the European shorthair cat (OR = 1). However, several breeds had significantly higher odds ratios (Fig. 15) (see Supplementary data).

Analyses of the influence of age revealed that the highest odds ratios of developing a tumour/malignant tumour in the mammary gland were in cats aged 8–16 years. Neutered and entire male cats had no significant differences in the odds of developing a tumour/malignant tumour in the mammary gland. Neutered female cats had significantly lower odds than entire female cats in both analyses. The odds of a female cat developing a tumour/malignant tumour in the mammary gland compared with a male cat were much higher (Table 2).

Gastrointestinal Tract

Of 18,375 diagnosed tumours, 1,373 (7.5%) were in the gastrointestinal tract. Of these, 1,196 (87.1%) were malignant. Due to the fact that benign tumours in the gastrointestinal tract were rare and had no important effect on the analyses, further investigations focused on malignant tumours only. The frequency of malignant tumours in the gastrointestinal tract compared with the overall tumour locations decreased from 1965 to 2008 (Fig. 16).

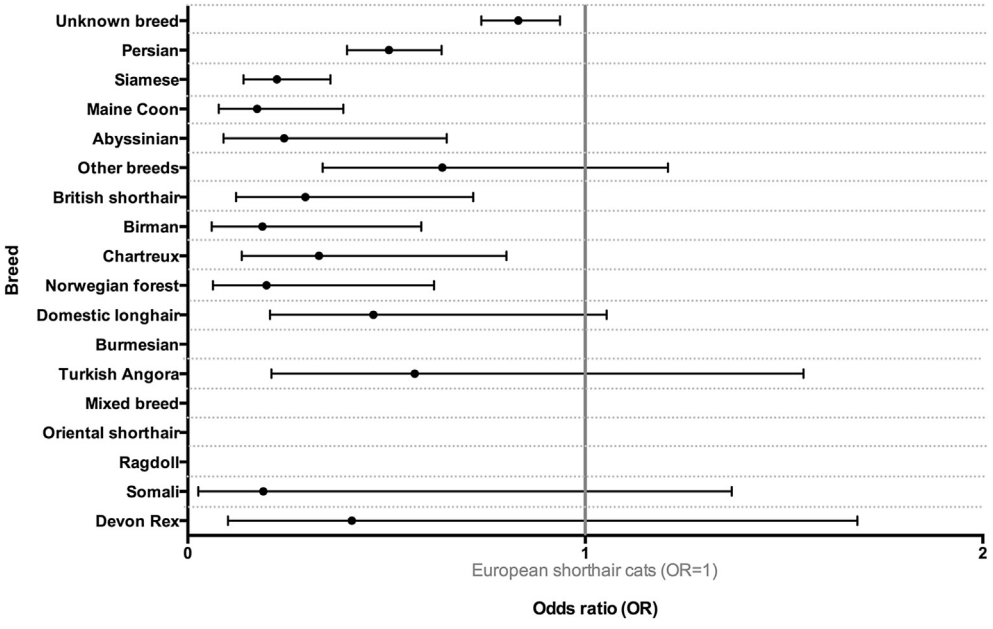

Fig. 10. Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common breeds that develop squamous cell carcinoma ($n = 1{,}811$) compared with the European shorthair cat (OR = 1).

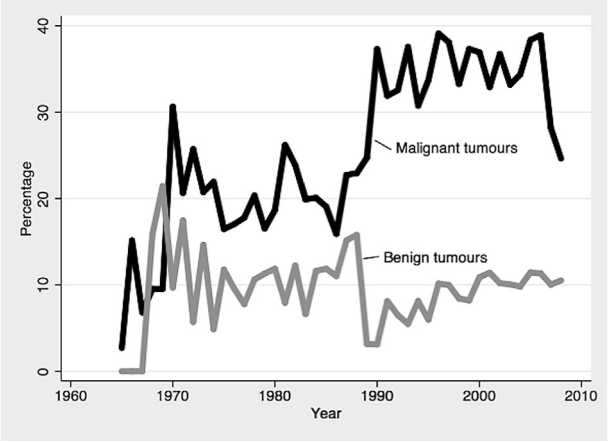

Fig. 11. Relative diagnosis frequency of skin and subcutaneous tumours expressed as a percentage of the overall tumour diagnoses between 1965 and 2008. Malignant tumours of the skin/subcutis ($n = 5{,}804$) and benign tumours of the skin/subcutis ($n = 1{,}825$).

Exploring in more detail the segments of the gastrointestinal tract: 50.2% of the malignant tumours were in the intestine, 27.8% in the liver and gallbladder, 13.6% in the pancreas, 6.3% in the stomach, 1.5% in the anal region and 0.75% in the oesophagus.

The most common malignant tumours in the gastrointestinal tract overall were adenocarcinomas and lymphoma (Fig. 17). In the intestine, the most common malignant tumours were lymphoma (40.7%), adenocarcinoma (40%) and sarcoma (7.3%).

Persian (OR = 0.64 [0.48, 0.84]) and Maine Coon (OR = 0.45 [0.22, 0.91]) cats had significantly lower odds of developing a malignant tumour in the gastrointestinal tract compared with the European shorthair cat (OR = 1). Siamese (OR = 1.45 [1.12, 1.87]) cats were the only breed with significantly higher odds (Fig. 18) (see Supplementary data). For evaluation of the intestine only: Siamese (OR = 1.92 [1.40, 2.64]), Chartreux (OR = 2.65 [1.39, 5.02] and Somali (OR = 3.41 [1.25, 9.36]) cats had significantly higher odds and Persian (OR = 0.5 [0.32, 0.76]) and Maine Coon (no tumour) cats had significantly lower odds of developing a malignant tumour in the intestine compared with European shorthair cats (see Supplementary data).

Analyses of the influence of age revealed that the odds of developing a malignant tumour in the gastrointestinal tract increased with age, with a mean age at diagnosis of 11.2 years. Cats aged 10–14 years (mean 10.8 years) had the highest odds of developing a malignant tumour in the intestine. The odds of a neutered cat developing a malignant tumour in the gastrointestinal tract were significantly higher compared with entire cats, for both males and females. There was no significant difference between the odds for female and male cats (Table 2). Analyses of intestinal tumours also revealed higher odds for neutered cats, but no significant differences in the male/female comparison (Table 2).

Cardiorespiratory System

Of 18,375 diagnosed tumours, 1,223 (6.7%) were in the cardiorespiratory system. Of these, 1,050 (85.9%) were malignant. Due to the fact that benign tumours in the cardiorespiratory system were rare and had no important effect on the analyses, further investigations focused on malignant tumours only. The frequency of malignant tumours in the cardiorespiratory system compared with overall tumour findings did not change substantially from 1965 to 2008 (Fig. 19).

Most malignant tumours of the cardiorespiratory system derived from the lung/bronchus (70.2%) and from the nasal cavity/middle ear (21.0%). The most common malignant tumours in the cardiorespiratory tract were adenocarcinomas, lymphomas and epithelial neoplasia NOS (Fig. 20).

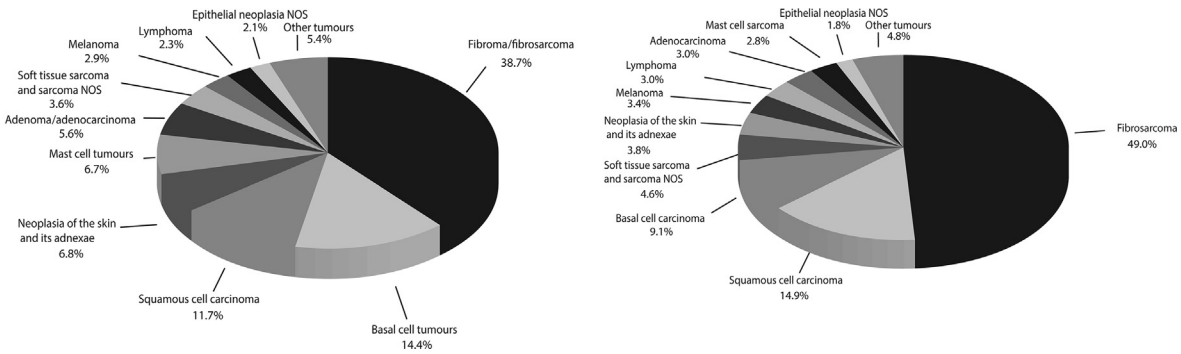

Fig. 12. Occurrence of the most common tumour types in the skin and subcutis. All tumours ($n = 7{,}629$; left) and malignant tumours ($n = 5{,}804$; right).

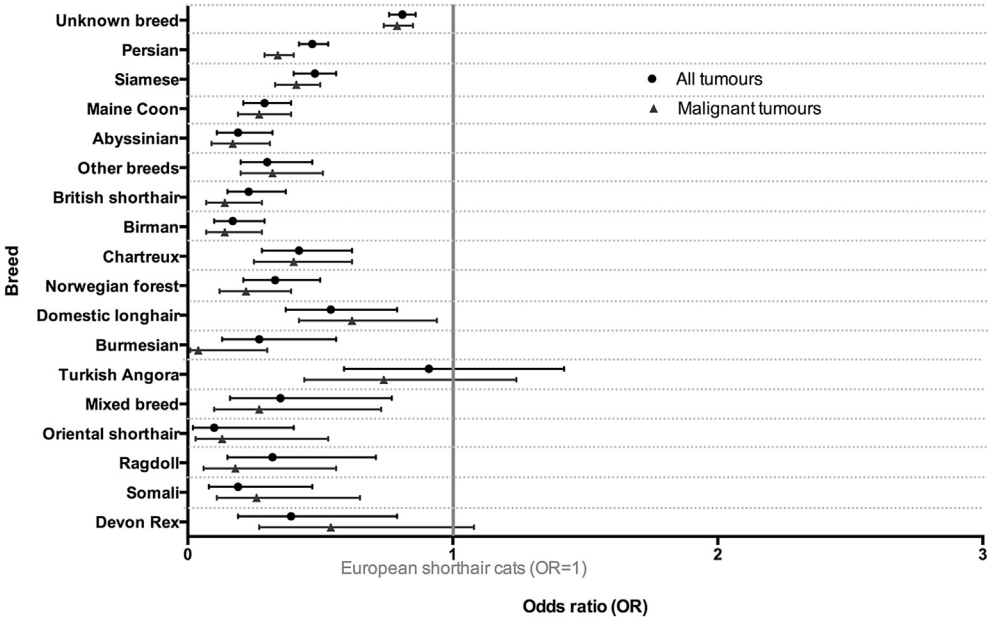

Fig. 13. Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common breeds that develop benign or malignant tumours ($n = 7{,}629$) or malignant tumours ($n = 5{,}804$) of the skin/subcutis compared with the European shorthair cat (OR = 1).

Evaluation of the lung/bronchus only showed that the most common malignant tumours were adenocarcinomas (48.3%), epithelial neoplasia NOS (22.1%) and lymphoma (13.6%).

No other breed had significantly higher odds of developing a malignant tumour in the cardiorespiratory system compared with the European shorthair cat (OR = 1). Abyssinian (OR = 0.24 [0.06, 0.95]) and Birman (OR = 0.13 [0.02, 0.92]) cats had significantly lower odds ratios (Fig. 21) (see Supplementary data). No significant breed differences were found in the location lung/bronchus.

Analyses of the influence of age revealed that the odds of developing a malignant tumour in the cardiorespiratory system increased with age. The same applied for the location lung/bronchus. The mean age of developing a tumour in the location lung/bronchus was 11.2 years.

The odds of a neutered cat developing a malignant tumour in the cardiorespiratory system were significantly higher compared with entire cats, for both

Table 2
Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common anatomical locations, where benign and malignant tumours or malignant tumours only were found, comparing sex and neutering status

Tumour location	*Male neutered versus male entire (OR = 1)*		*Female neutered versus female entire (OR = 1)*		*Female versus male (OR = 1)*	
	OR (95% CI)	*P*	*OR (95% CI)*	*P*	*OR (95% CI)*	*P*
Skin and subcutis*	1.06 (0.98, 1.15)	0.15	1.18 (1.1, 1.28)	0.00	1.04 (0.98, 1.09)	0.18
Skin and subcutis†	1.08 (0.99, 1.18)	0.10	1.26 (1.15, 1.37)	0.00	1.07 (1.01, 1.14)	0.02
Skin*	1.09 (1.00, 1.20)	0.06	1.12 (1.03, 1.23)	0.01	1.00 (0.94, 1.07)	0.90
Skin†	1.13 (1.01, 1.27)	0.03	1.21 (1.08, 1.35)	0.00	1.04 (0.97, 1.12)	0.27
Mammary gland*	0.75 (0.46, 1.2)	0.23	0.62 (0.55, 0.7)	0.00	21.17 (16.68, 26.86)	0.00
Mammary gland†	0.86 (0.51, 1.5)	0.63	0.69 (0.61, 0.79)	0.00	21.85 (16.73, 28.54)	0.00
Gastrointestinal tract†	1.81 (1.50, 2.18)	0.00	1.55 (1.29, 1.87)	0.00	0.92 (0.82, 1.04)	0.19
Intestine†	1.61 (1.25, 2.07)	0.00	1.36 (1.05, 1.76)	0.02	0.87 (0.74, 1.03)	0.1
Cardiorespiratory system†	1.95 (1.57, 2.43)	0.00	1.91 (1.56, 2.32)	0.00	1.17 (1.03, 1.32)	0.02
Lung/bronchus†	2.35 (1.78, 3.11)	0.00	2.22 (1.75, 2.82)	0.00	1.28 (1.11, 1.49)	0.00
Oral cavity/pharynx†	1.31 (1.05, 1.62)	0.02	1.35 (1.08, 1.69)	0.01	0.84 (0.73, 0.96)	0.01

*All tumours.
†Malignant tumours.

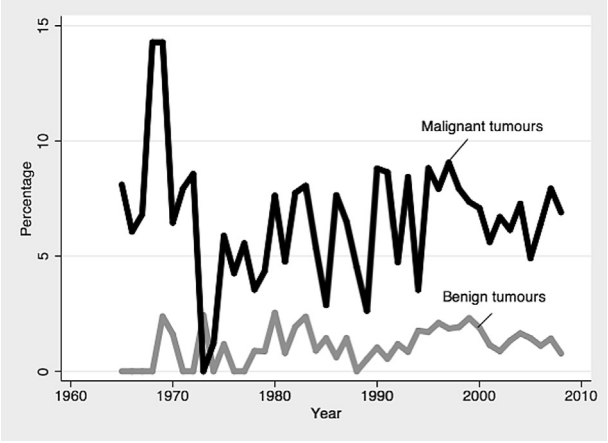

Fig. 14. Relative diagnosis frequency of mammary tumours expressed as a percentage of overall tumour diagnoses between 1965 and 2008. Malignant mammary tumours ($n = 1{,}249$) and benign mammary tumours ($n = 252$).

males and females. The odds of a female cat developing a malignant tumour in the cardiorespiratory system compared with a male cat were significantly higher. The same was true for the location lung/bronchus (Table 2).

Oral Cavity and Pharynx

Of 18,375 diagnosed tumours, 980 (5.3%) were in the oral cavity/pharynx. Of these, 862 (88.0%) were malignant. Due to the fact that benign tumours in the oral cavity/pharynx were rare and had no important effect on the analyses, further investigations focused on malignant tumours only. In the 1970s and 1980s, the frequency of malignant tumours in the oral cavity/pharynx compared with overall tumour findings ranged between 0 and 4%. In the 1990s their frequency increased and the relative frequencies have remained between 3 and 7% ever since (Fig. 22).

The most common malignant tumours in the oral cavity/pharynx were squamous cell carcinoma and fibrosarcoma (Fig. 23).

No other breed had significantly higher odds of developing a malignant tumour in the oral cavity/pharynx compared with the European shorthair cat (OR = 1). Unknown breed (OR = 0.82 [0.69, 0.99]), Siamese (OR = 0.45 [0.26, 0.75]) and Abyssinian (OR = 0.14 [0.02, 0.98]) cats had significantly lower odds ratios (Fig. 24) (see Supplementary data).

Analyses of the influence of age revealed that the odds of developing a malignant tumour in the oral cavity/pharynx increased with age, with a mean age at diagnosis of 12.2 years. The odds of a neutered cat developing a malignant tumour in the oral cavity/pharynx were significantly higher compared with an entire cat, for both males and females. The odds of female cats developing a malignant tumour in the oral cavity/pharynx compared with male cats were significantly lower (Table 2).

Discussion

This study provides a more in-depth evaluation of data contained within the Swiss Feline Cancer

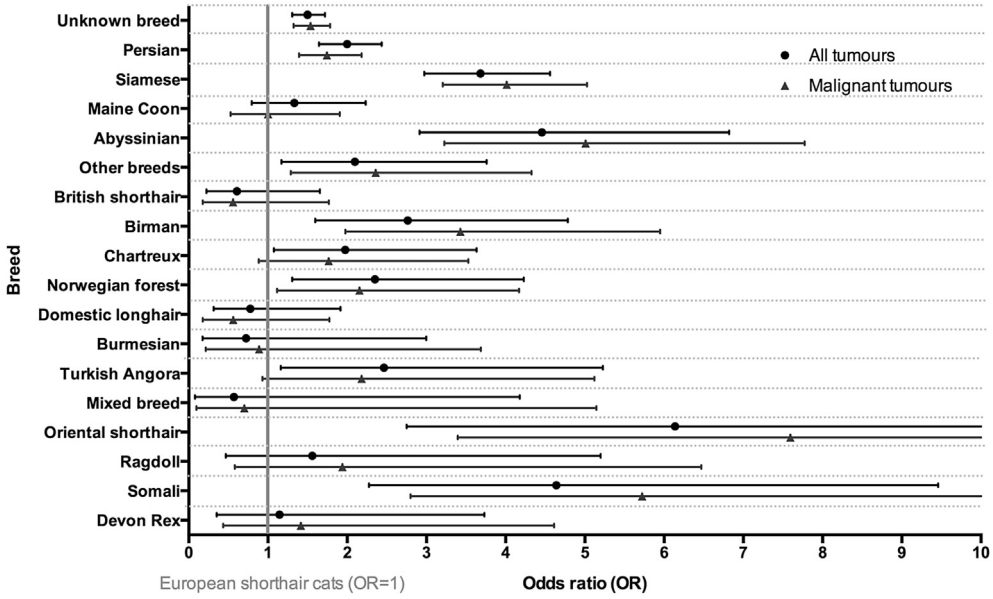

Fig. 15. Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common breeds that develop a tumour (benign and malignant, $n = 1{,}501$) in the mammary glands or a malignant tumour ($n = 1{,}249$) in the mammary glands compared with the European shorthair cat (OR = 1).

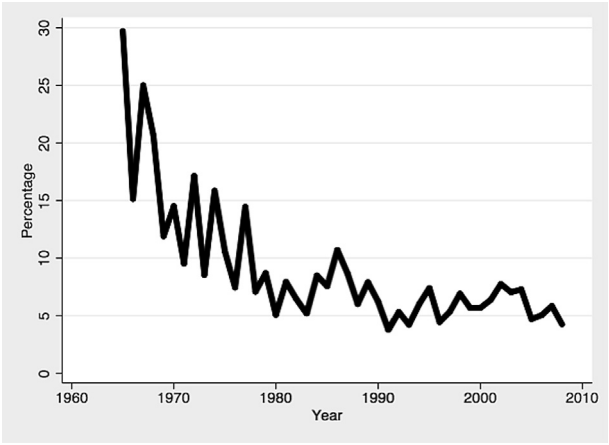

Fig. 16. Relative diagnosis frequency of malignant tumours in the gastrointestinal tract ($n = 1{,}196$) expressed as a percentage of overall tumour diagnoses between 1965 and 2008.

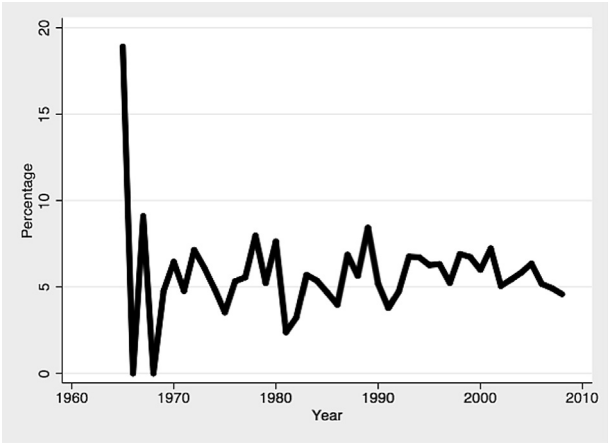

Fig. 19. Relative diagnosis frequency of malignant tumours in the cardiorespiratory system ($n = 1{,}050$) expressed as a percentage of overall tumour diagnoses between 1965 and 2008.

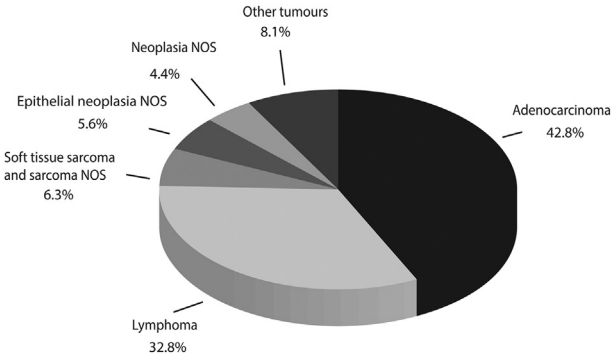

Fig. 17. Occurrence of the most common malignant tumour types ($n = 1{,}196$) in the gastrointestinal tract.

Registry. The most common tumour types and their locations were analysed with respect to possible influential variables, tumour distribution and frequency over the period of study. Only results where comparisons with other studies are possible will be discussed. However, it should be kept in mind that other registries have often used different methodologies, inclusion criteria, tumour classifications and statistical evaluations and comparisons should be interpreted with caution. On the other hand, the data collected in this study derive from a large number of samples, which could explain why in some instances previously unrecognized risk factors were uncovered. Another reason for discrepancies with previous studies could

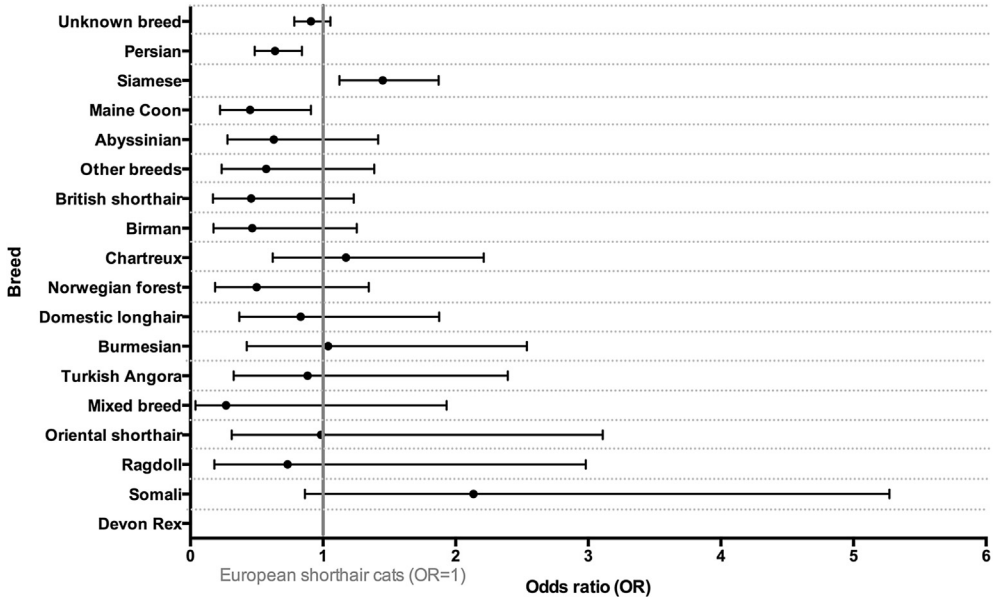

Fig. 18. Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common breeds that develop a malignant tumour of the gastrointestinal tract ($n = 1{,}196$) compared with the European shorthair cat (OR = 1).

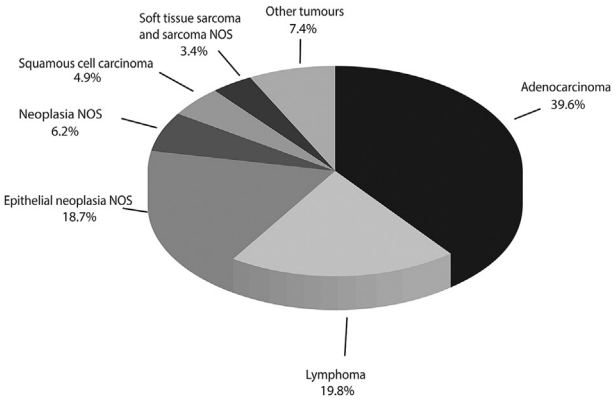

Fig. 20. Occurrence of the most common malignant tumour types ($n = 1{,}050$) in the cardiorespiratory system.

derive from true differences in the genetic structure of the Swiss cat population as compared with the populations of other studies.

Probably the most interesting results with respect to the possible aetiology of tumours relate to the frequencies of fibrosarcoma and lymphoma in this study. Between 1965 and 1990, the frequency of fibrosarcomas increased from 0% to around 10% of the overall tumour diagnoses. In the 1990s, fibrosarcoma frequency increased to approximately 20% and has remained stable ever since. A number of studies have revealed an association between the use of injectable products, including vaccines against rabies and feline leukaemia virus (FeLV) and the development of sarcomas located at injection sites (feline injection site sarcomas) (Hendrick and Goldschmidt, 1991; Hendrick *et al.*, 1992, 1994; Kass *et al.*, 1993; Macy and Hendrick, 1996). The inactivated animal rabies vaccine was developed in the 1950s and 1960s (Cabasso *et al.*, 1965; Dietzgen and Kuzmin, 2012). The first FeLV vaccine became available in Switzerland in 1986 (Lutz, 1986). The substantial increase in sarcomas, which started in the 1990s, might therefore be related to the introduction of the FeLV vaccine in Switzerland.

The data show that fibrosarcomas occurred more frequently in middle-aged and older cats. There was a small difference between sex and neutering status. Significant differences were found between breeds. Some breeds had odds of developing a fibrosarcoma that were more than five times lower than those of the European shorthair cat. Existing studies found that fibrosarcomas mostly occur in older cats, with no breed or sex predilection (Miller *et al.*, 1991; Goldschmidt and Shofer, 1992). The present study is the first to reveal significant differences in the development of fibrosarcomas in cats of different sex and breed. This could be due to the high number of animals in the study; however, further studies are necessary to confirm these differences.

From the 1970s to the beginning of the 1990s, lymphoma was fairly frequent (up to 38%) compared with other tumour types. In the 1990s, its frequency decreased to around 10%. Many lymphomas were caused by FeLV (Jarrett *et al.*, 1964; Hardy, 1980). The decrease in the frequency of lymphomas in the

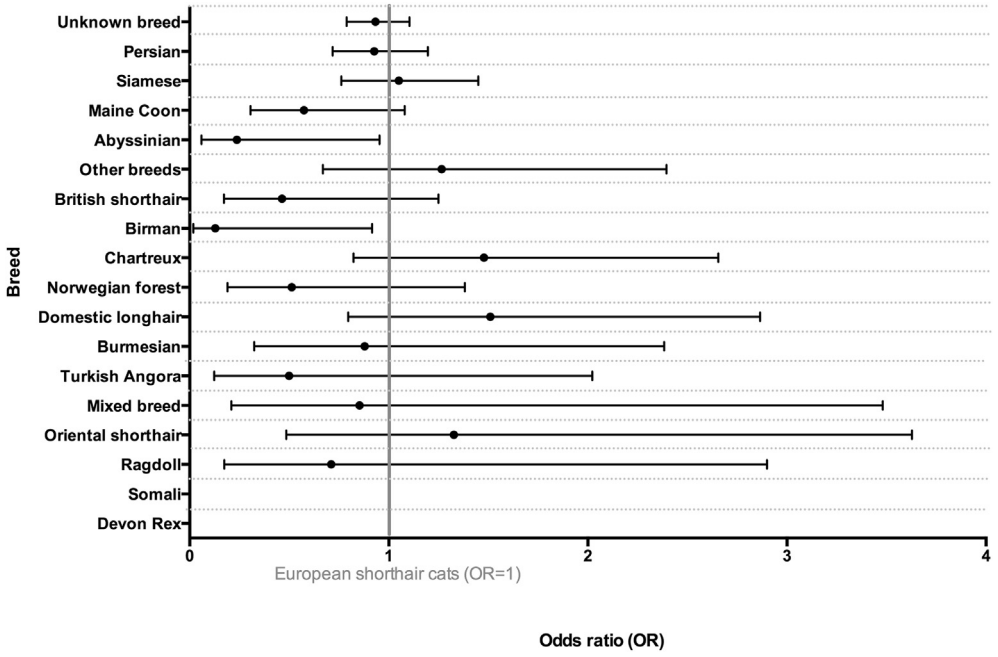

Fig. 21. Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common breeds that develop a malignant tumour in the cardiorespiratory system ($n = 1{,}050$) compared with the European shorthair cat (OR = 1).

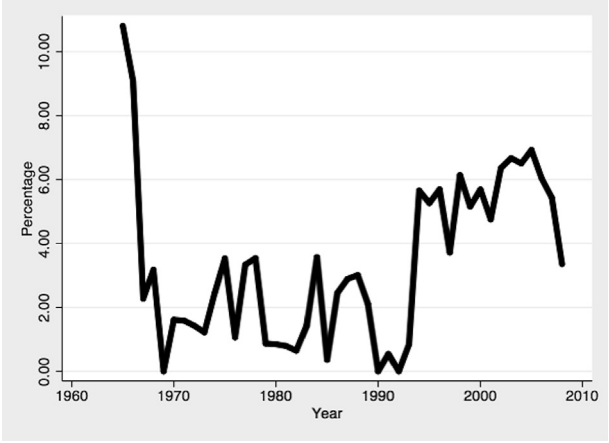

Fig. 22. Relative diagnosis frequency of malignant tumours in the oral cavity/pharynx ($n = 862$) expressed as a percentage of overall tumour diagnoses between 1965 and 2008.

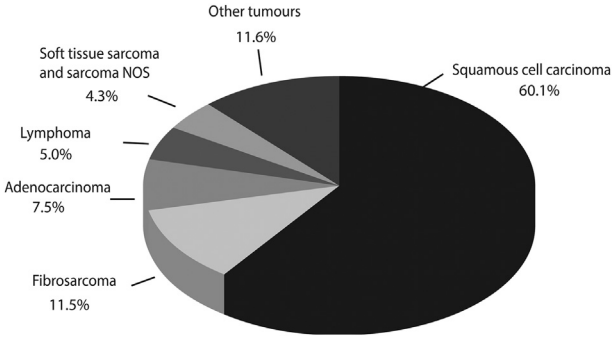

Fig. 23. Occurrence of the most common malignant tumour types in the oral cavity/pharynx ($n = 862$).

1990s could therefore be explained by the introduction of the FeLV vaccine into Switzerland (Lutz, 1986).

The results show that the mean age for developing lymphoma was 8.5 years. Contrary to other tumours, lymphomas were also frequent in young cats. Neutered cats had higher odds of developing lymphoma compared with entire cats and male cats had higher odds than females. Oriental shorthair and Somali were the only breeds with a significantly higher odds ratio than that of European shorthair cats.

Studies carried out in North America (Meincke *et al.*, 1972; Hardy, 1981), Australia (Sabine *et al.*, 1974) and Japan (Haga *et al.*, 1988) found that lymphoma occurs at mean ages of 4–6 years. More recent studies carried out in Australia (Court *et al.*, 1997; Gabor *et al.*, 1998) and North America (Vail *et al.*, 1998; Louwerens *et al.*, 2005) determined mean ages between 8 and 11 years. High incidences of lymphoma among young cats have also been described in other studies (Dorn *et al.*, 1968b; Sabine *et al.*, 1974; Gabor *et al.*, 1998). A predisposition of males has been described in some studies (Dorn *et al.*, 1968b; Court *et al.*, 1997; Gabor *et al.*, 1998; Vail *et al.*, 1998), while no association was found in others (Meincke *et al.*, 1972; Haga *et al.*, 1988). No predisposition of neutered cats has been described.

Siamese/Oriental breeds were found to be overrepresented in some studies (Court *et al.*, 1997; Gabor *et al.*, 1998; Louwerens *et al.*, 2005), while no breed prevalence was found in others (Haga *et al.*, 1988). However, because of limited numbers of animals,

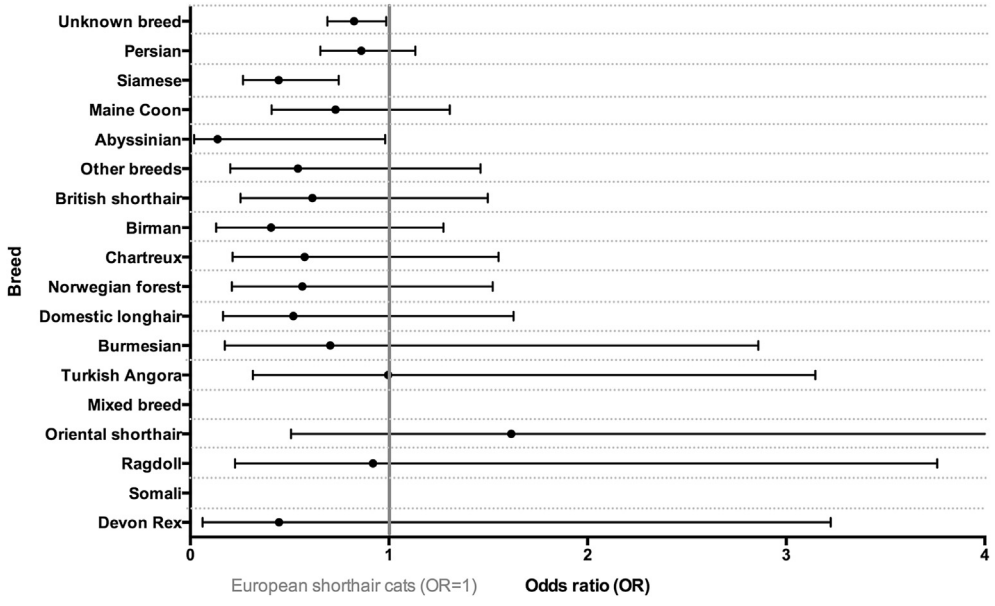

Fig. 24. Odds ratios (ORs) and 95% confidence intervals (CIs) for the most common breeds that develop a malignant tumour in the oral cavity/pharynx ($n = 862$) compared with the European shorthair cat (OR = 1).

Siamese cats were pooled in a group with the Oriental breeds in these studies.

Comparing the present data with other existing studies on the most common tumour types in cats, data on cutaneous tumours are in general agreement (Bostock, 1986; Stiglmair-Herb, 1987; Jörger, 1988; Miller *et al.*, 1991). We show a higher frequency of fibrosarcomas compared with the other study carried out in Switzerland in 1988. This is due to the increase in fibrosarcomas in the 1990s. In Germany, the frequency of fibrosarcomas was already high (43%) in 1987 (Stiglmair-Herb, 1987).

A lower frequency of lymphomas in the gastrointestinal tract was seen in the present study compared with others (Cotchin, 1952; Patnaik *et al.*, 1975; Rissetto *et al.*, 2011). The reason for the relatively small number of lymphomas in the gastrointestinal tract could be because information on the location of most lymphomas was missing. Another reason could be that these tumours might have been classified as something other than lymphoma when the tumour involved viscera other than the intestine.

Adenocarcinoma as the most frequent tumour type in the lung/bronchus and squamous cell carcinoma as the most frequent tumour type in the oral cavity/pharynx have also been described by other investigators (Patnaik *et al.*, 1975; Dorn and Priester, 1976; Stebbins *et al.*, 1989; Hahn and McEntee, 1997; Meuten, 2002; D'Costa *et al.*, 2012).

The high number of cats and the long study period in the present investigation allowed us to show the relative frequency of feline tumours over time. To our knowledge, there is no other study that has published comparable numbers. Changes in frequency could reveal environmental influences. However, the time-dependent differences in the prevalence of certain tumours, particularly those with an irregular course, may reveal biases in changed detection methods or success in countermeasures/preventive measures, such as vaccination. Further studies and analysis would elucidate such courses in detail.

The frequency of tumour development increases with age for all tumour types and tumour locations. Mean ages calculated in the present study all correspond well with the mean ages calculated in other studies (Cotchin, 1952, 1961; Dorn *et al.*, 1968b; Hayden, 1971; Weijer *et al.*, 1972; Stuenzi *et al.*, 1974; Patnaik *et al.*, 1975; Hayes *et al.*, 1981; Moulton *et al.*, 1981; Stiglmair-Herb, 1987; Jörger, 1988; Stebbins *et al.*, 1989; Ito *et al.*, 1996; Hahn and McEntee, 1997; Rissetto *et al.*, 2011).

The present study revealed higher odds of developing a tumour in neutered cats than in entire cats for many tumour types and tumour locations; however, differences were sometimes very small. Higher odds in entire cats compared with neutered cats were only found for females and mammary gland tumours.

Few studies have analysed the differences between neutered and entire cats except for investigations of mammary neoplasia. The increased risk for neoplasia in this organ system in entire cats has been described in several studies. The benefit of neutering appears to be dependent on the age at which the procedure is performed (Dorn *et al.*, 1968b; Hayes *et al.*, 1981; Misdorp *et al.*, 1991; Overley *et al.*, 2005). Cotchin (1952) and Rissetto *et al.* (2011) described a higher risk for neutered animals of developing a tumour in the intestine. We found that females had higher odds compared with males of developing adenomas/adenocarcinomas (all tumours and malignant tumours only) and tumours in the skin/subcutis (malignant tumours), mammary gland, cardiorespiratory system and lung/bronchus. Males had higher odds compared with females for the oral cavity/pharynx.

Other studies found no sex differences for squamous cell carcinoma (all locations) and for all tumours in the skin/subcutis (Cotchin, 1961; Stiglmair-Herb, 1987; Jörger, 1988). Sex predilection is controversial regarding feline gastrointestinal, lung/bronchus and oral cavity/pharyngeal tumours. Some studies note a male overrepresentation in gastrointestinal tumours and others report equal representation between the sexes (Cotchin, 1952; Patnaik *et al.*, 1975; Turk *et al.*, 1981; Rissetto *et al.*, 2011). Higher frequencies in females were found by Patnaik *et al.* (1975) in the lung/bronchus and oral cavity/pharynx. Equal rates were described by D'Costa *et al.* (2012) and Dorn *et al.* (1968b).

In contrast to the higher number of patient records in the present study, other studies grouped feline breeds according to a limited numbers of case records. Only approximate comparisons are therefore possible. In the present study, several breeds had much lower odds ratios for developing squamous cell carcinoma compared with European shorthair cats. Miller *et al.* (1991) found that Siamese cats had fewer squamous cell carcinomas than expected, although this difference was not statistically significant. An increased risk in European shorthair and a decreased risk in Siamese, Himalayan and Persian cats was reported by Goldschmidt and Hendrick (2002).

In the present study, several breeds had significantly higher odds ratios for developing a tumour in the mammary gland compared with the European shorthair cat. The highest odds ratios were shown for Oriental shorthair, Somali, Abyssinian and Siamese cats. An overrepresentation among Siamese cats was described by two other studies (Hayes *et al.*, 1981; Ito *et al.*, 1996).

Siamese cats had significantly higher odds of developing a malignant tumour of the gastrointestinal tract and Siamese, Chartreux and Somali cats had

significantly higher odds of developing a tumour in the intestines compared with the European shorthair cat. An overrepresentation among Siamese cats was described in several studies (Patnaik *et al*., 1975; Turk *et al*., 1981; Cribb, 1988; Rissetto *et al*., 2011).

No breed predisposition was found for tumours of the lung/bronchus. No breed predispositions were reported in other studies, except for one that described Persian cats as being overrepresented (D'Costa *et al*., 2012).

In conclusion, this study has focused on the most frequent tumour types and tumour locations diagnosed in cats between 1965 and 2008 and the possible influence of sex, age and breed. The sampling period of more than 40 years allowed us to construct a comprehensive retrospective feline cancer registry. Compared with existing studies of feline tumours, most results are similar, but some contradict other studies and for some results there was no comparison. Since in many studies different methodologies, inclusion criteria, tumour classifications and statistical analyses were used, it would be desirable to define for future studies, international standards for animal cancer registries.

Acknowledgments

We gratefully acknowledge the help of the IVPZ staff, D. Erni, N. S. Schenker and G. Lott, during collection and processing of primary data and all colleagues of the Collegium Helveticum, who contributed in various ways. We are grateful to the veterinary practitioners who submitted cases over a long period of time, which made this and further studies possible. Finally, we greatly appreciate H. Murray's revision of the English version. This study was financed through the financial support of the University of Zurich to A. Pospischil for acting as a fellow at the Collegium Helveticum during his fellowship period of 2009–2016.

Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jcpa.2016.01.008.

Conflict of Interest Statement

The author(s) declare(s) no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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[*Received, October 22nd, 2015*
Accepted, January 22nd, 2016]