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## Incidence of pyometra in Swedish insured cats<sup>☆</sup>



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### ABSTRACT

Pyometra is a clinically relevant problem in intact female cats and dogs. The etiology is similar in both animal species, with the disease caused by bacterial infection of a progesterone-sensitized uterus. Here, we studied pyometra in cats with the aim to describe the incidence and probability of developing pyometra based on age and breed. The data used were reimbursed claims for veterinary care insurance or life insurance claims or both in cats insured in a Swedish insurance database from 1999 to 2006. The mean incidence rate (IR) for pyometra was about 17 cats per 10,000 cat years at risk (CYAR). Cats with pyometra were diagnosed at a median age of 4 years and a significant breed effect was observed. The breed with the highest IR (433 cats per 10,000 CYAR) was the Sphynx, and other breeds with IR over 60 cats per 10,000 CYAR were Siberian cat, Ocicat, Korat, Siamese, Ragdoll, Maine coon, and Bengal. Pyometra was more commonly diagnosed with increasing age, with a marked increase in cats older than 7 years. The mean case fatality rate in all cats was 5.7%, which is slightly higher than corresponding reports in dogs of 3% to 4%. Geographical location (urban or rural) did not affect the risk of developing the disease. The present study provides information of incidence and probability of developing pyometra based on age, breed, and urban or rural geographical location. These data may be useful for designing cat breeding programs in high-risk breeds and for future studies of the genetic background of the disease.

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### 1. Introduction

Pyometra is a clinically relevant problem in female cats and dogs. Almost 20% of female intact dogs experienced pyometra by 10 years of age [1]. The clinical presentation of pyometra is similar in cats and dogs, with symptoms as vaginal discharge, anorexia, and lethargy most commonly described [2,3]. Also the etiology is perceived as similar with progesterone influence predisposing the uterus for uterine bacterial infection, which can be life-threatening [4–6]. No prevalence data for pyometra have so far been described in cats, but observations of most veterinarians

are that the disease is observed less commonly than in dogs. For example, Dow [5] reported a ratio of one cat to three dogs diagnosed with pyometra in his clinical practice; moreover, at the University Animal Hospital, Swedish University of Agricultural Sciences, Uppsala, Sweden, 15 cats were diagnosed with pyometra during 1 year compared with about 175 dogs (data not shown) [7]. The difference in occurrence has been suggested to depend on the fact that cats mainly are induced ovulators and therefore less exposed to progesterone influence and subsequently also have lower risk of the disease [8]. The disease risk varies significantly among dog breeds, and in certain breeds more than 50% of female dogs contracted pyometra before 10 years of age [1,9,10]. It is not known if the incidence rate (IR) varies among different cat breeds because the overall occurrence in cats has not been studied. In Sweden, about 30% of cats are purebred

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(Manimalisrapporten 2005, <http://www.manimalis.se/uploads>). The majority of Swedish cats are spayed/neutered, reportedly as many as 70% ([11]). It is not known how large the proportion of neutered individuals is in purebred cats compared with in non-pedigree cats.

Cat breeding is becoming increasingly popular in Sweden, with at present 33 different cat breeds registered, and overall morbidity and mortality has recently been reported based on breed [12–14]. Many of these breeds are numerically small, but even breeds that are numerically larger often have low numbers of breeding animals [12–14]. This may be due to a large number of neutered cats, a wish by the owners to avoid contact with other cats or a restrictive selection of suitable breeding animals. Consequently, the genetic pool may become narrow in several cat breeds, which can cause problems due to inbreeding. However, the effect of inbreeding within breeds and the genetically different cat breeds may also present research opportunities. Because cats and humans often are affected by similar diseases, genetic studies of disease-causing mutations in cats may greatly facilitate subsequent studies also in humans, as has previously been described for dogs [15–21]. Thus, studies in cats are likely to be valuable for future disease prevention, health, and welfare, not only for their own species. A prerequisite for such genetic studies is identification of the disease incidence in different cat breeds.

The Swedish insurance database (Agria Insurance, SE, Stockholm, Sweden; [www.agria.se](http://www.agria.se)) has been used to describe the patterns of mortality in life-insured cats and morbidity in cats with veterinary care insurance [12,14]. The aim of the present study was to describe the incidence and probability of developing pyometra with respect to age, breed, and geographical location. The data used were reimbursed claims for veterinary care insurance or/and life insurance claims in female cats insured at the Agria insurance company during the period from 1999 to 2006.

## 2. Materials and methods

### 2.1. Description of the insurance process from 1999 to 2006

In general, only purebred cats have life insurance, usually acquired at young age, although cats can enter life insurance until 6 years of age. Cats can enter a veterinary care-insurance program at any age, but life insurance is only valid till the age of 13 years. If cats are more than 2 or 6 years when first insured, for life and veterinary care insurance, respectively, applications must be accompanied by a veterinary health certificate. For veterinary care insurance, there is a predetermined deduction (in the year 2003, it was 1200 SEK (when 100 SEK ~ \$80US and ~90 Euro)) for a claim period (i.e., 100 days), whereas the median premium was 450 SEK, and for most cats the maximum reimbursement within a year to animal owners was 30,000 SEK. After a veterinary visit, the receipt for veterinary care costs is submitted to the insurance company (electronically or by mail). When a life-insured cat dies, a claim is processed using forms completed by the attending veterinarian, including a summary of the cat's disease problems,

and if requested by the insurance company, the complete medical record. In general, in the insurance computer database only one diagnostic code is used per claim, codes which are made by attending veterinarians. In general, the study populations were a large population of cats with veterinary care insurance, a much smaller population of life-insured cats, and an even smaller population of cats with both insurance types simultaneously.

### 2.2. Data management

Data on all cats insured between 1999 and 2006 were downloaded from the insurance database. All female cats were included in the analysis as timing of neutering was not reliable in the database. Variables used in this study included cat identification, sex, date of birth, breed, life insurance coverage, and diagnostic codes for receipts for veterinary care insurance and life insurance claims. Dates of visits to veterinarians and when cats entered or left the insurance program and reasons for leaving insurance were included. Cats were assigned to the age category they belonged to on 1st January of each year ( $0 < 1$  years,  $1 < 2$ , etc.). Dates of visits to veterinarians, when cats entered or left the insurance program, and reasons for leaving insurance were also included.

In the insurance data, 41 breed codes were used to classify breeds. Breeds that were considered closely related were combined: Abyssinians and Somalis were combined to Abyssinians; Persians, Chinchilla, colourpoint Persians, and Exotic shorthairs to the Persian group; and Siamese, Balinese, Foreign White, Javanese, Oriental shorthair, and Seychelliosis to the Siamese group. Data have been presented for individual breeds with at least 1000 cat years at risk (CYAR). "Domestic" cats included domestic shorthair and longhair cats. The group described as "other" included various breeds.

### 2.3. Diagnosis

Veterinarians classify medical problems and diseases using a standardized hierarchical diagnostic registry, including both specific and general codes (Swedish Animal Hospital Association, diagnostic registry for the horse, the dog, and the cat, Taberg, 1993, in Swedish). The selected diagnostic code was pyometra, that is, not including cases of hydrometra or mucometra.

### 2.4. Data analysis

Two data sets were created. One consisted of all cats with veterinary care insurance and cats were included when less than 13 years old. The other "combined" data set consisted of cats with both veterinary care and life insurance (<13 years old). In both these data sets, cats with at least one reimbursed receipt for claimed insurance, with a relevant diagnosis submitted to the insurance company contributed to the numerator for morbidity; that is, for the first data set, the cases was only for veterinary care, whereas in the combined data set, the claims could be of either insurance type or both. For one insurance type (life insurance), the case fatality, that is, the proportion

**Table 1**

Cat years at risk (CYAR), in years, for female cats with veterinary care insurance and with coverage of both veterinary care and life insurance.

Variable	Category	CYAR veterinary care	n (cats)	CYAR veterinary care and life	n (cats)
Total		462,374	139,075	66,721	23,771
Breed	Abyssinian group	4087	1180	2520	869
	American Curl	6	7	5	4
	Asian	15	5	5	2
	Bengal	941	477	691	377
	Birman	21,585	5721	13,069	4126
	Domestic cat	329,263	101,044	3201	1050
	Bombay	44	16	33	12
	British shorthair	5349	1587	3166	1090
	Burma	4404	1112	2482	773
	Burmilla	77	24	83	25
	Cornish Rex	3230	1022	1858	727
	Devon Rex	2397	710	1701	595
	Egypt Mau	7	2	3	2
	European shorthair	20,358	4604	766	228
	Japanese Bobtail	0	1	0	1
	Korat	237	56	152	37
	LaPerm	0	1	0	0
	Maine coon	4578	1612	3060	1281
	Manx	322	82	52	18
	Norwegian forest cat	17,917	5263	8911	3116
	Ocicat	1064	320	749	272
	Other breeds	1687	695	718	373
	Peterbald	1	1	1	1
	Pixie Bob	0	0	0	0
	Ragdoll	3379	1415	2648	1257
	Rex	330	100	166	63
	Russian Blue	1921	488	1096	304
Selkirk Rex	0	2	0	1	
Siamese group	6976	2032	3925	1392	
Sibirian cat	402	238	385	221	
Sphynx	165	125	154	112	
Turkish Van	377	104	195	60	
Persian group	31,054	8979	14,838	5355	
Location	Rural	256,634	80,070	40,464	14,926
	Urban	205,740	59,005	26,256	8845

with claimed life insurance due to pyometra, was determined.

Cats were at risk from either 1<sup>st</sup> January 1999 or the start date of insurance (if later), and until the date of the first relevant veterinary care claim, of death, or of withdrawal from insurance. Incidence calculated from disease claims over the entire time-period cats were insured and contributing to the CYAR was explored rather than prevalence because of disease characteristics where pyometra occurs in the majority of cases as a single event. Incidence rate calculations were performed with the exact time at risk (CYAR) as the denominator. Rates are expressed as cats (cases with at least one event) per 10,000 CYAR. Standard errors times 1.96 yielded 95% confidence intervals (95% CIs) for IRs. In general, nonoverlapping 95% CIs have been used as evidence of statistical difference, mainly comparing rates within the respective categories for breed and geographical location (rural vs. urban). Case age (first event) has been described using 5th, 50<sup>th</sup>, and 95th percentiles. The probability of acquiring pyometra at a certain age (i.e., 1-survival to the first event) was constructed using stratified Cox proportional hazards regression without covariates. The smooth macro was then used to transform the baseline survival into age-specific hazards (Allison P: Survival analysis using the SAS system: a practical guide; Cary,

1995). Data handling was performed by SAS version 9.1 (SAS Institute Inc., Cary, NC, USA).

### 3. Results

#### 3.1. The cat population studied

The number of female cats that were insured for veterinary care during the study period was 139,075 cats and the total number of CYAR 462,374. The number of female cats with both veterinary care and life insurance was 23,771 and total number of CYAR was 66,721 (Table 1).

#### 3.2. Pyometra

The number of female cats reimbursed for pyometra was 791 in the veterinary care population, and the mean IR thus 17 per 10,000 CYAR. The IR varied significantly by breed, from five in the Russian blue to 433 in the Sphynx (Tables 2 and 3), but did not depend on whether cats lived in urban or other areas. The median age of diagnosis was 4 years; the IR increased with age and was more pronounced after 7 years of age (Fig. 1). In total, 19 of 335 cats died because of pyometra, leading to a mean case fatality rate of 5.7% in the population calculated from the combined data set.

**Table 2**

Number of cats, incidence rates (IRs) with 95% confidence intervals (95% CI), and median age of cases for cats with pyometra that were registered for veterinary care or for both veterinary care and life insurance coverage (age data derived from veterinary care data in cats without additional life insurance).

Variable	Category	Insurance form												
		Veterinary care						Veterinary care and life insurance						
		Cases (cats)	IR	95%	CI	Median	Case age, percentiles		Cases (cats)	IR	95%	CI	Deaths	Case fatality (%)
							5th	95th						
Overall		791	17	16	18	4	1	11	335	50	45	56	19	5.7
Breed	Sphynx	7	433	112	754	1	1	4	5	330	41	620	0	–
	Siberian cat	5	125	15	234	2	1	4	5	130	16	245	0	–
	Ocicat	11	105	43	168	2	1	5	8	108	33	183	0	–
	Korat	2	86	–33	204	5	1	10	1	66	–63	195	0	–
	Siamese group	58	84	63	106	2	1	10	48	124	90	160	0	–
	Ragdoll	27	80	50	111	2	1	4	20	76	43	109	1	3.7
	Maine coon	31	68	44	92	2	1	7	21	70	40	99	2	6.5
	Bengal	6	64	13	116	3	1	6	4	60	1	115	0	–
	Devon Rex	14	59	28	90	5	1	11	9	53	18	88	0	–
	Burma	23	53	31	74	2	1	8	14	57	27	87	0	–
	Turkisk Angora	1	52	–50	154	7	7	7	0	0		0	0	–
	Cornish Rex	16	50	26	75	4	1	13	11	60	24	95	0	–
	Norwegian forest cat	69	39	30	48	3	1	10	38	43	29	57	3	4.3
	Birman	75	35	27	43	3	1	11	65	50	38	62	5	6.7
	Persian group	104	34	27	40	4	1	11	62	42	32	52	7	6.7
	British shorthair	17	32	17	47	3	1	11	11	35	14	56	0	–
	Rex	1	31	–29	90	9	9	9	0	0		0	0	–
	Abyssinian group	11	27	11	43	2	1	11	7	28	7	49	0	–
	Other breeds	2	12	–5	28	8	3	12	2	28	–11	67	0	–
	European shorthair	23	11	7	16	9	2	12	1	13	–13	39	0	–
	Domestic cat	287	9	8	10	6	1	12	1	3	–3	9	0	–
	Russian Blue	1	5	–5	15	4	4	4	2	18	–7	44	1	100
Location	Urban	364	18	16	20	4	1	11	192	48	46	64	3	0.8
	Rural	427	17	15	18	4	1	11	143	55	41	55	16	11.9

**Table 3**

Proportion of cats with pyometra (%) diagnosed before 13 years of age in selected breeds.

Breed	Pyometra (%)
All breeds	2.2
Norwegian forest cat	14.8
Birman	3.1
Persian group	3.4
Siamese group	8.8
Domestic cat	0.9

The data set included data from cats at least insured for veterinary care that were analyzed by Cox proportional hazard regression analysis without covariates.

#### 4. Discussion

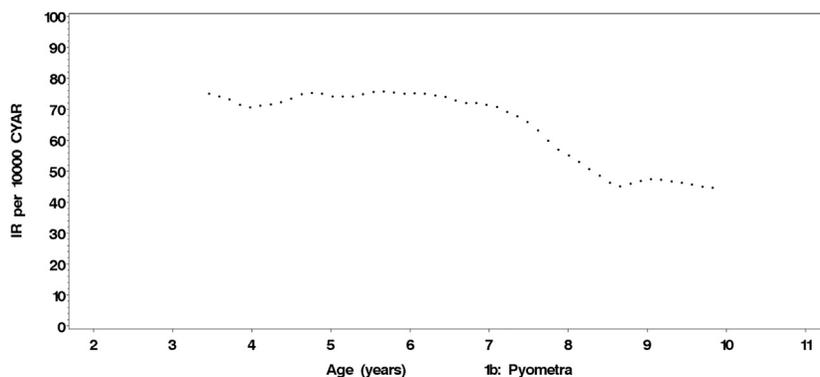
The overall IR of pyometra was 17 cats per 10,000 CYAR in the study population. Importantly, a significant difference in the risk for developing pyometra among cat breeds is described for the first time. The breed with the highest IR (433 cats per 10,000 CYAR) was the Sphynx, and other breeds with IR over 60 cats per 10,000 CYAR were Siberian cat, Ocicat, Korat, Siamese, Ragdoll, Maine coon, and Bengal. In some of these breeds, only a few individuals were insured, which may affect the accuracy of the IR. Overall, 2.2% of cats experienced the disease by 13 years of age, but this proportion varies from 0.9% in mixed breed cats to the Norwegian forest cat with 14.1%. The reason why many Norwegian forest cats are diagnosed with pyometra by 13 years of age and Birman or Persian group cats are not in spite of having similar IRs is unclear. Genetic factors are likely to affect the disease risk, as indicated by the breed differences observed in the present study. As in dogs, pyometra was more common with increasing age, with a marked increase in cats older than 7 years [9]. This pattern, with the disease mainly occurring later in life, is in agreement with earlier reports [5,17].

Pyometra is a disease of the middle-aged or older animal. The mean age of pyometra diagnosis was 4 years in our study. This is similar to a previous report [6] but different from the median age of 7.2 years in another [2]. Because clear differences in breed and age exist, variations between different studies may depend on the selection of cats

included in each study population. The present study is the only one based on the cat population at large which minimizes such effects. A small peak in the curve displaying IRs was observed after 9 years of age (Fig. 1). It could be speculated whether this increase is related to degenerative changes in the uterus or other conditions such as ovarian pathologies or uterine neoplasia that more often affect older animals and may predispose for developing pyometra. Uterine neoplasia is rare in cats, with a median age for diagnosis of 9 years, but it has been described also in younger cats [18–20]. Endometrial hyperplasia, on the other hand, is common in older cats, and this condition is regarded as potentially precancerous in humans [17,21]. Expression of the HER-2/neuoncoprotein, which is associated with proliferation and has prognostic importance for human endometrial cancer, was increased in the endometrium and glandular epithelium of uteri from cats with pyometra in one study [21]. Unless histological examination is performed, less severe neoplastic conditions of the uterus may be undetected because inflammatory uterine wall enlargement could appear macroscopically similar. Whether pyometra and neoplasia are induced simultaneously as has been observed in some cats or whether neoplasia precedes pyometra or *vice versa* remains to be determined [18–21].

The case fatality for pyometra overall was 5.6%. In dogs it is reported to be 3% to 4% [9]. The reason for the higher fatality rate in cats is not known, but one theory could be that this species is less sensitive to endotoxin, or not as prone to show clinical signs unless they develop sepsis [6,22]. In cats showing only mild signs of disease, admission to a veterinary clinic relatively late in the disease progression could potentially lead to a less favorable outcome [2]. This could also explain why many cats show only mild signs of disease [2]. If the uterus ruptures, subsequent septic bacterial peritonitis may lead to mortality rates up to 31% to 57%, which is why pyometra should be considered a serious and potentially life-threatening condition [6,23,24].

Pyometra develops as a consequence of repeated progesterone exposure during the luteal phase of the estrus cycle. Progesterone makes the uterine environment suitable for fetal development by promoting gland growth and mucus secretion, decreasing muscular activity, and



**Fig. 1.** Age-specific incidence rate (IR) for first event/reimbursement claim of pyometra for female cats at least insured for veterinary care (not life) during 1999 to 2006. CYAR, cat years at risk.

suppressing leukocyte function in the uterus [25]. These effects of progesterone are potentiated by estrogen [26]. In cats, pyometra is likewise associated with progesterone influence because most cats with pyometra have CL present in the ovaries [5]. Administration of contraceptive drugs or presence of repeated spontaneous ovulation in cats, which is known to occur even if the cat has induced ovulation, may, therefore, potentially increase the risk of developing pyometra [27]. Regarding the other reproductive hormone estrogen, one study proposed that continuous estrogen stimulation could be a central contributor to the development of the disease in cats [17]. Continuous estrogen stimulation chiefly induces endometriosis in women and the development of pyometra in cows [28,29]. Breeders should take all these factors into consideration. Further investigations are necessary, however, to completely understand the complex etiology and pathogenesis.

Diagnostic information for cats has been validated and been found to be correctly coded in 84% of scrutinized records, and data on breed, age, and sex (only male/female) were correctly coded to an even greater extent [30]. The diagnosis of pyometra is clinically distinct, and the correctness is therefore expected to be high. There is no reason to believe that the insurance coverage differs among cat breeds; but in Sweden, purebred cats are insured to a larger extent than non-pedigree cats [12–14]. The non-pedigree cats in the present study can thus be assumed to represent a proportion of domestic cats that are cared for to a larger extent than the general domestic cat, which should be kept in mind when comparing data between purebred and non-pedigree cats. The two populations, the “only veterinary care” and the “combined,” were included to achieve a means to extrapolate as broad as possible, as well as to determine the total disease load and case fatality in the population with a more full coverage. Even if the estimates for the both populations agree well, they are not directly comparable because the numerators are different.

A drawback is the generally high proportion of spayed/neutered animals. The spay/neuter status has a known effect on all diagnoses of the reproductive tract or associated with reproductive hormones. More purebred than non-pedigree cats can be expected to be used as breeding animals for a longer time, and thus not be castrated or be castrated at an older age; but to our knowledge, there are no data to support this. If more non-pedigree cats are castrated at a younger age, this would obviously decrease the risk for pyometra in these cats. The comparisons between breeds for purebred cats are less likely to be greatly affected by spay/neuter frequencies because it is unlikely that the proportion of spay/neutered cats varies extensively among breeds. Generally, most cat owners have insurance for veterinary care only, and it is possible that the cats that have combined insurance have a somewhat higher proportion of unneutered animals because owners (e.g., mostly breeders) consider their animal valuable and also want to have coverage for life insurance. The insurance routines are not likely to be altered during the study period because there was no changes in neuter routines or the insurance process during these years.

In a previous study using the same database, the rate of at least one veterinary care event was generally higher in

urban compared with other areas [12]. Whether this was attributed to true differences in disease risk or variation in breed distributions or owner's attitude or a function of the availability and cost of veterinary services was beyond the scope of that study. In the present study, IRs did not differ between urban compared with other areas for pyometra, suggesting that environmental causes probably have little effect on this disease. The data reported here are likely applicable to other countries with similar insurance costs and management routines. Age was normalized to 1st January, resulting in the possible bias of cats born late in the year could be introduced into an older age category at time of diagnosis but would be similar for all breeds studied.

In humans, endometrial hyperplasia, neoplasia, and infection of the uterus are serious problems [31–33]. Pyometra is less commonly diagnosed, but is regarded as a serious condition [34]. Mammary pathologies in cats have been proposed as useful models for studies on the human counterparts [35]. Being a severe bacterial infection, pyometra could serve as a natural disease model for uterine infection and possibly also for sepsis [6,23,36–39]. Endometrial cancer is the most common gynecological cancer in humans with increasing mortality rates due to the lack of early diagnostic biomarkers, and studies of uterine proliferative conditions in cats may contribute valuable information [21,40,41]. Furthermore, many single-nucleotide polymorphisms (SNPs) have now been mapped across the cat genome, and will thus allow for the development of SNP genotyping platforms for mapping feline diseases [42]. In dogs, it has been described that genome-wide association mapping of Mendelian traits can be achieved with as few as about 20 dogs of each breed [15]. Genetic studies comparing cat breeds with varying IR are thus likely to be useful for minimizing the occurrence of certain diseases by adapted cat breeding programs. The results could also facilitate subsequent identification of the genetic background and pathogenesis of the corresponding diseases in humans.

#### 4.1. Conclusions

The present study provides information of the incidence and probability of developing pyometra based on age, breed, and geographical location. The mean IR of pyometra was about 17 cats per 10,000 CYAR with a significant breed effect observed. The median age at diagnosis was 4 years, and the disease was more commonly diagnosed with increasing age. The mean case fatality rate in all cats was 5.7%. These data may be useful for designing cat breeding programs in high-risk breeds and lays a foundation for further studies of the genetic background of the disease.

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Author contributions: RH drafted the article. AE performed the statistical analyses. All authors participated in the design and coordination of the study and helped to draft the article. All authors read and approved the final article.

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