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Disease patterns in 32,486 insured German shepherd dogs in Sweden 1995 2006

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The aims of this retrospective study were to describe the morbidity and mortality in German shepherd dogs (GSD) in Sweden, based on insurance data, and to test the hypothesis that GSDs are predisposed to immune-related diseases. Morbidity was defined as incidence rates and based on veterinary care events. Mortality was defined as mortality rates and based on life insurance data. The study included 445,336 dogs, 7.3 per cent GSDs, covered by both veterinary care and life insurance between 1995 and 2006 in the Swedish insurance company Agria (Agria Insurance Company, Stockholm, Sweden). For veterinary care events (morbidity) GSDs were most over-represented for immunological disease, with a relative risk (RR) of 2.7, compared with the risk in all other breeds combined. The most common disease category (morbidity) in GSDs was skin disorders with an incidence rate of 346.8 cases per 10,000 dog years at risk. The highest RR for cause of death in GSDs compared with all other breeds was for skin conditions (RR=7.8). Locomotor disorders were the most common cause of death in GSDs. The GSD is predisposed to immune-related disorders, such as allergies, circumanal fistulae and exocrine pancreatic atrophy, with significantly increased risk compared with all other breeds.

Introduction

Population-based studies on disease patterns in companion animals are scarce since it is difficult to obtain accurate population-level estimates from records presented by veterinary clinics. Much of our understanding of the occurrence of diseases in dogs is based on case reports, which lack information about the si e and composition of the population at risk. D atabases from animal health insurance companies contain information on the background populations, as well as clinical events, making them useful in epidemiological research.

A large proportion of the Swedish dog population is covered by an insurance plan. A bout one-third of the Swedish purebred dog population is insured in the insurance company A gria (genvall and others 1998) which offers insurance covering costs for veterinary care and life insurance. M ost dogs insured for veterinary care also have a life insurance policy. G enerally, coverage for veterinary care is valid for dogs less than 12 years old, whereas the life insurance pays out if the dog dies before the age of 10 years. T he A gria database is validated as a useful tool for epidemiological research of overall morbidity and mortality, as well as specific diseases in dogs (onnett and others 1997). M any published population-based studies in dogs are based on this register (onnett and others 1997, 2005, genvall and others 2000a, b, c, 2005, onnett and genvall 2010,).

Information about the most common diseases and causes of death for a certain breed can help to set priorities for preventive measures. T he G erman shepherd dog (G SD) is one of the most popular working and companion dog breeds worldwide, and one of the three most common breeds in Sweden. T he overall disease pattern in G SD s is not well described, and a population-based study would therefore provide valuable information both in general and for designing and interpreting intervention studies. T he primary aim of this study is to describe the disease patterns for morbidity and mortality in G SD s in Sweden, based on insurance data from the years 1995 2006. T his will include determination of the most common disorders within the breed, as well as a comparison with other breeds in order to identify disorders where the G SD is relatively over-represented. A secondary aim is to test the hypothesis that G SD s are predisposed to immune-related diseases.

Material and methods
Study population

A gria offers two kinds of insurance plans for dogs. ne is for veterinary care in which the owner, in the event of disease, is reimbursed for costs exceeding the deductible for veterinary visits (veterinary care events). T he other is a life insurance plan in which the owner is reimbursed a specific amount specified by the policy in case of death caused by disease or accident. T he insurance process, as well as the breed distribution in the database, has earlier been described in detail (genvall and others 2000a, b).

D ata on all dogs insured between anuary 1, 1995 and D ecember 31, 2006 were downloaded from the A gria insurance database. nly disease episodes in which the excess of cost is exceeded within the claim period were recorded in the claims database. V ariables used in this study included dog identification, sex, breed, date of birth, diagnostic code(s), dates of visits to veterinarians and when dogs entered or left the insurance programme. Sex was either male or female. o information was available on neuter status.

T he study population consisted of 445,336 dogs enrolled in both veterinary care and life insurance before 12 months of age between 1995 and 2006 in A gria, 32,486 (7.3 per cent) of these were G SD s

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(16,500 males and 15,986 females). T he mortality data included dogs enrolled in life insurance between 1995 and 2006. T he morbidity data included dogs enrolled in veterinary care insurance during the period 1995 2006. D ogs were observed until they died, withdrew from insurance, or until the end of the observation period, D ecember 31, 2006.

riefly describing the diagnostic process, attending veterinarians classify the medical problems using a standardised diagnostic registry (Swedish A nimal ospital rganisation 1993), including both specific and general codes in hierarchical order. In general, only one diagnostic code is used per claim. For purposes of this study, the original diagnosis (provided by the veterinarian) was then collated into specific and then more general categories of diagnoses. For example, the original diagnosis of acute external otitis would be included in the specific diagnosis category otitis externa and in the general category ear . T he 24 general disease categories made during the analysis are based on body system or disease process, for example, skin , locomotor , immunological , neoplasia and gastrointestinal (see the complete list of general categories in T able 1). T he specific diagnoses include diagnoses such as atopy or gastroenteritis , but also symptomatic definitions such as itching , lame without further specification and symptom of disease with no established cause, cutis, subcutis. In this study, data were presented in the general disease categories, as well as by more specific diagnoses. A s an illustration of the organisation of the diagnostic categories used in this study, Table 2 presents the subdivisions of allergy in the general disease category immunological .

Statistical analyses

A retrospective longitudinal cohort study was performed using Swedish insurance data from 1995 to 2006. T he morbidity in G SD s insured in A gria was calculated as true incidence rates (IR) where the denominator was the sum of each animal s total time in the register and number of disease events, where only the first claim for each dog within each general or specific category was included, was the numerator. T he IR were multiplied by 10,000 and presented as number of events per 10,000 dog years at risk (D A R).

T he mortality in G SD s insured in A gria was calculated as mortality rates (M R) where the number of deaths were divided by the sum of each animal s total time in the register. M R were multiplied by 10,000 to be interpreted as the number of deaths per 10,000 D A R. It is not possible to distinguish between death and euthanasia in these data, and we used the terms interchangeably in this report.

TA L 2 Subdivisions of the group allergic in the general disease category (level 3) immunological				
Level 3	Level 2	Level 1	Specific diagnosis	riginal diagnosis
Immunological	Allergic	Allergy atopy	Allergy atopy	Allergy with involvement of skin rticaria angioderma Contact dermatitis allergy Food allergy Drug allergy ormonal hypersensitivity ypersensitivity to parasites, bacteria and insects Allergy to fleas ypersensitivity to parasites
		Atopy yposensitisation	Atopy yposensitisation
	Anaphylactic shock	Anaphylactic shock	Anaphylactic shock, whole animal
		ronchitis asthma	ronchitis asthma	Allergic bronchitis (asthma)
	Symptom of allergic disease	Symptom of allergic disease	Symptom of allergic disease

oth M R and IR in G SD s were compared with those for all other breeds (combined) and presented as relative risk (R R). T he diseases and disease groups in which G SD s were over-represented in regard to morbidity or mortality, were described in more detail with a description of age and sex distribution of specific diagnoses. Standard error multiplied by 1.96 yielded 95 C I for IR , M R and mean ages and G SD s were considered to have a significant difference for the comparison for conditions where the C Is did not overlap those for all other breeds. Significant differences in the proportion of males and females within conditions (diagnoses) was detected using Proc Fre and the exact two-sided binomial test (SA S).

T he analysis was done using the software package SA S V .9.3 (SA S Institute, C ary, orth C arolina, SA).

Results
Morbidity

Table 1 presents the mean age at first claim and the IR for the general cause of veterinary care events, and Fig 1 presents the R R , where 1 is the risk in all other breeds. G SD s were most over-represented for immune-related disease with a R R of 2.7 (Fig 1) and the average age at first claim for a G SD was 3.5 years (Table 1). T he most common general disease category in G SD s was skin disorders with an incidence rate of 346.8 cases per 10,000 D A R (Table 1), and with almost twice the risk compared with all other breeds (Fig 1). T he average age at first claim for dermatologic disorders in a G SD was 4.2 years.

Table 3 presents specific diagnoses within the general category skin , where itching was the most common specific diagnosis with an incidence rate of 98.4 cases per 10,000 D A R . A mong the 10 most common specific diagnoses within the general group skin in G SD s, circumanal fistulae had highest R R . T his diagnosis had 46 times higher incidence rate in G SD s compared with all other breeds. C ircumanal fistulae was more common in males (P < 0.0001) and the mean age at first claim was 6.1 years (Table 3).

Table 4 shows the most common specific causes for veterinary care in G SD s. A topy was the specific diagnosis with the highest R R , being 3.6 times more common than in other breeds. T he mean age at the first atopy-claim was 3.3 years. Pyometra was the most common specific diagnosis in G SD s with an incidence rate of 98.9 cases per 10,000 D A R , approximately the same as in other breeds in general. T he second and third most common specific diagnoses were itching and lame without further specification , respectively (Table 4).

TA L 1 General causes for veterinary care in GSDs		
	Mean age first claim, GSD ears (95 CI)	IR, GSD Cases 10 000 D AR (95 CI)
Skin	4.2 (4.1 to 4.3)	346.8 (336.8 to 356.8)
Locomotor	4.1 (4.0 to 4.2)	295.4 (286.2 to 304.6)
Gastrointestinal	4.2 (4.1 to 4.3)	267.1 (258.3 to 275.9)
In ury	3.5 (3.4 to 3.6)	236.6 (228.4 to 244.8)
eoplasia	7.1 (7.0 to 7.2)	230.8 (222.7 to 239.0)
Reproductive female	6.0 (5.9 to 6.2)	160.6 (153.8 to 167.4)
Symptom whole body	5.2 (5.0 to 5.3)	145.9 (139.4 to 152.4)
ar	4.6 (4.4 to 4.7)	116.1 (110.3 to 121.9)
Respiratory upper	3.0 (2.8 to 3.1)	114.2 (108.5 to 120.0)
Immunological	3.5 (3.4 to 3.6)	83.1 (78.2 to 88.0)
Infection	4.5 (4.4 to 4.7)	79.8 (75.0 to 84.5)
Reproductive male	6.3 (6.1 to 6.4)	56.9 (52.8 to 60.9)
rinary lower	4.8 (4.5 to 5.1)	47.5 (43.8 to 51.2)
yes	4.4 (4.2 to 4.7)	47.1 (43.4 to 50.8)
eurological	5.8 (5.5 to 6.1)	34.7 (31.5 to 37.8)
eart	6.0 (5.6 to 6.5)	17.7 (15.5 to 20.0)
Respiratory lower	5.1 (4.6 to 5.6)	16.7 (14.5 to 18.9)
ndocrine	6.6 (6.3 to 7.0)	15.1 (13.0 to 17.2)
lood vascular	6.6 (6.1 to 7.0)	15.0 (12.9 to 17.1)
Surgery complication	5.1 (4.7 to 5.6)	12.3 (10.4 to 14.1)
rinary upper	5.5 (5.0 to 6.1)	12.0 (10.1 to 13.8)
Claw	5.7 (5.0 to 6.4)	5.3 (4.1 to 6.5)
Respiratory thoracic	4.9 (3.6 to 6.1)	2.5 (1.6 to 3.3)
ehaviour	4.0 (3.0 to 5.0)	1.9 (1.2 to 2.7)

Ranked by incidence rate (IR)
Total number of GSDs 32,486 dogs (16,500 males and 15,986 females)
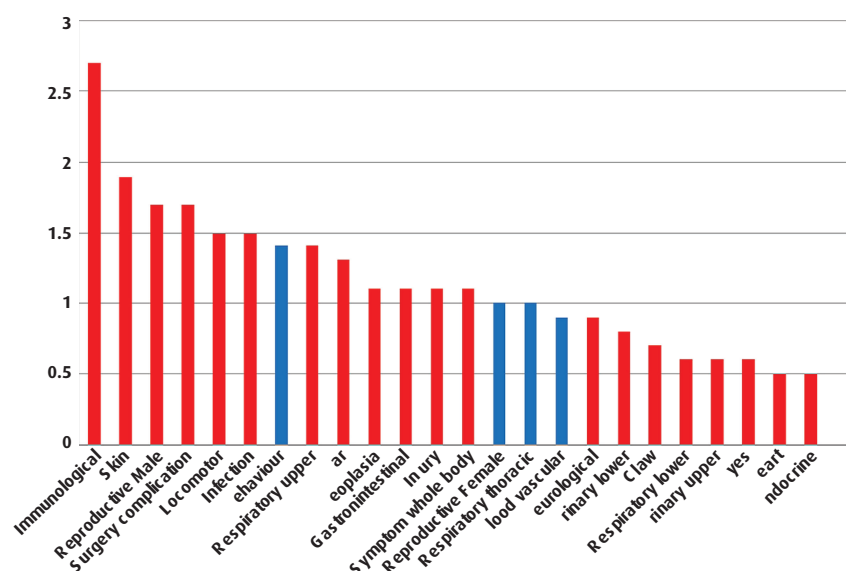D AR, dog years at risk GSD, German shepherd dog

FIG 1 Relative Risk (RR) for general causes for veterinary care in the German shepherd dog (GSD) compared with all other breeds. ((Incidence rate (IR) in breed) IR all other breeds)). Disease categories with a significant difference (non-overlapping CI intervals) between IRs in GSDs and all other breeds have red bars. ote The distance between the RRs 0.5 and 1.0 e uals the distance between 1.0 and 2.0

TA L 3 Ten most common diagnoses within the general category skin for veterinary care in GSDs			
	Mean age first claim, GSD ears (95 CI)	IR, GSD Cases 10,000 D AR (95 CI)	RR
Itching	3.5 (3.3 to 3.6)	98.4 (93.1 to 103.8)	2.6
Acute anal sack inflammation	4.6 (4.4 to 4.8)	44.7 (41.1 to 48.3)	1.2
Symptom of disease with no established cause, cutis, subcutis	3.9 (3.6 to 4.1)	42.5 (39.0 to 46.0)	2.2
eratoacanthoma	6.0 (5.8 to 6.3)	33.6 (30.5 to 36.7)	2.7
Acute dermatitis of unknown origin	4.5 (4.2 to 4.8)	31.8 (28.8 to 34.9)	2.0
Superficial acute pyoderma	4.5 (4.2 to 4.8)	28.5 (25.6 to 31.3)	2.4
Circumanal fistulae	6.1 (5.8 to 6.3)	25.5 (22.8 to 28.2)	46.0
Acute inflammatory condition, cutis, subcutis	4.7 (4.3 to 5.1)	20.0 (17.6 to 22.4)	1.7
ot spot	3.9 (3.5 to 4.3)	15.5 (13.4 to 17.6)	1.3
Abscess, cutis, subcutis	5.1 (4.6 to 5.6)	12.8 (10.9 to 14.7)	1.1
Ranked by incidence rate (IR) Total number of GSDs 32,486 dogs (16,500 males and 15,986 females) Diagnoses with a significant difference (non-overlapping CI intervals) between IRs in GSDs and all other breeds. D AR, dog years at risk GSD, German shepherd dog RR, relative risk			

TA L 4 15 most common diagnoses (all categories) for veterinary care in GSDs			
	Mean age first claim, GSD ears (95 CI)	IR, GSD Cases 10,000 D AR (95 CI)	RR
Pyometra	6.8 (6.6 to 6.9)	98.9 (93.6 to 104.2)	1.0
Itching	3.5 (3.3 to 3.6)	98.4 (93.1 to 103.8)	2.6
Lame (without further specification)	3.8 (3.7 to 4.0)	97.2 (91.9 to 102.5)	1.5
eoplastic changes, cutis, subcutis	6.0 (5.8 to 6.2)	85.3 (80.3 to 90.2)	1.1
Acute external otitis	4.2 (4.1 to 4.4)	84.1 (79.2 to 89.0)	1.3
Tumour in the udder	8.2 (8.1 to 8.3)	79.5 (74.8 to 84.3)	1.3
Acute tonsillitis	2.6 (2.4 to 2.7)	69.7 (65.2 to 74.1)	1.7
roken tooth	4.3 (4.0 to 4.5)	46.2 (42.6 to 49.8)	2.4
Acute anal sack inflammation	4.6 (4.4 to 4.8)	44.7 (41.1 to 48.3)	1.2
Cuts, cutis, subcutis	2.7 (2.6 to 2.9)	44.2 (40.6 to 47.7)	2.2
ites, cutis, subcutis	3.5 (3.2 to 3.7)	43.9 (40.3 to 47.4)	1.1
Acute gastroenteritis	3.6 (3.3 to 3.8)	43.2 (39.7 to 46.7)	1.1
Symptom of disease with no established cause, cutis, subcutis	3.9 (3.6 to 4.1)	42.5 (39.0 to 46.0)	2.2
Atopy	3.3 (3.2 to 3.5)	42.2 (38.8 to 45.7)	3.6
Symptom of tiredness	4.9 (4.7 to 5.2)	35.6 (32.4 to 38.8)	1.2
Ranked by incidence rate (IR) Total number of GSDs 32,486 dogs (16,500 males and 15,986 females) Diagnoses with a significant difference (non-overlapping CI intervals) between IRs in GSDs and all other breeds. D AR, dog years at risk GSD, German shepherd dog RR, relative risk			

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Immune-related diagnoses

T he immune-related diagnoses were the diagnoses represented in the general disease category immunological , and these were divided into three ma or groups allergic , autoimmune and various immune-related diseases. T he IR and M R for these three groups are presented in Table 5. A llergic disease had the highest R R regarding morbidity, G SD s were 3.1 times more likely to have at least one veterinary care event for allergic compared with other breeds, as well as highest incidence rate in G SD s, 71.2 cases per 10,000 D A R. Five hundred and sixty-five (59 per cent) of the 953 dogs in the group allergic had been further diagnosed as affected by atopy , see Table 4. T he mean age at first claim, 3.3 years, does not differ between the specific diagnosis atopy and the group allergic . A llergic is also the group of immune-related diseases where the mortality rate in G SD s is highest, 12.8 deaths per 10,000 D A R. It was 6.3 times more common that a G SD died was euthanased due to allergic disease, when compared with all other breeds. T here was a significant difference in the sex distribution among the autoimmune disorders, where males were over-represented (P=0.04). T his male predominance was represented by lupus-disorders (P=0.02). T he other disorders included in the category autoimmune , for example, autoimmune blood disorders (ie, autoimmune haemolytic anaemia) and autoimmune skin disease (ie, pemphigus), had no significant difference in sex distribution.

Including some diagnoses that are suspected to be immune-related, but not included in the category immunological , there are some breed-specific diseases, such as exocrine pancreatic insufficiency (PI), G erman shepherd dog pyoderma and circumanal fistulae. Sixty-seven per cent of the cases were males and the mean age at first claim was 5.8 years. A nother disease where the G SD was strongly over-represented is PI with a RR of 32.5. T he diagnosis was first made at an average age of 3.6 years, and the cases were evenly distributed between the sexes. T he eye disorder pannus was 16 times more common in G SD s compared with all other breeds, and the mean age at first claim was 6.3 years. C hronic eosinophil gastroenteritis and chronic lymphocytic plasmacytic enteritis belongs to the inflammatory bowel disease (I D) syndrome, and these diagnoses were 1.5 and 1.9 times more common in G SD s, however, these diagnoses are represented by rather few cases. ypothyrosis is a diagnosis where

the G SD was under-represented, and for demodex ust slightly over-represented (T able 6).

Mortality

ut of the 445,336 dogs in the study population, 46,922 dogs (11.1 per cent G SD s) were euthanased or died during the study period, and each was assigned a diagnosis for cause of death. Skin is the general category where the G SD was most over-represented with a R R of mortality at 7.8 compared with other breeds (Fig 2). C ircumanal fistulae was the specific skin diagnosis with the highest mortality rate (16.0 deaths per 10,000 D A R), as well as the highest R R of mortality. It was 87.9 times more common that circumanal fistulae was the cause of death in G SD s compared with all other breeds. D eep chronic pyoderma was the fifth most common skin disorder causing death in G SD s, the diagnosis was 6.9 times more common in G SD s compared with other breeds (T able 7).

L ocomotor disorders were the most common cause of death in G SD s. T he mortality rate was 117.6 cases per 10,000 D A R (Table 8). T his was 3.4 times higher than for all other breeds (Fig 2). T he mean age at death was 4.6 years in G SD s (Table 8). T he ma or specific diagnosis within the locomotor category were hip dysplasia and degenerative lumbosacral stenosis . D egenerative lumbosacral stenosis was 16.0 times more common in G SD s compared with other breeds, and the mean age at death was 7.0 years. ip dysplasia as a cause of death was 8.0 times more common in G SD s than in other breeds, and the mean age at death was 2.7 years (T able 9).

L ooking at the specific diagnoses for mortality in G SD s, PI was the fifth most common cause of death with a mortality rate of 13.7 deaths per 10,000 D A R. As with morbidity, G SD s had a strong predisposition to this diagnosis regarding mortality with a relative mortality risk of 44.4 times higher than all other breeds. T he mean age at death for G SD s euthanased due to PI was 3.9 years. A topy was the seventh most common specific cause of death with a mortality rate of 7.9 deaths per 10,000 D A R , and a RR at 7.3 compared with all other breeds. T he mean age at death for G SD s euthanased due to atopy was 4.3 years (Table 9).

TA L 5 Immune-related diagnoses from the general category Immunological

	Mean age at first claim, GSD ears (95 CI)	IR, GSD morbidity Cases 10,000 D AR (95 CI)	RR, morbidity	MR, GSD Mortality Deaths 10,000 D AR (95 CI)	RR, mortality
Allergic	3.3 (3.2 to 3.5)	71.2 (66.7 to 75.8)	3.1	12.8 (10.8 to 14.9)	6.3
Autoimmune	5.6 (5.0 to 6.3)	5.4 (4.1 to 6.6)	1.1	0.5 (0.1 to 0.9)	1.2
Various immune related diseases	4.8 (4.0 to 5.5)	3.7 (2.7 to 4.8)	1.7	2.5 (1.6 to 3.4)	1.7

Morbidity and mortality in GSDs. Ranked by incidence rate (IR)
Total number of GSDs 32,486 dogs (16,500 males and 15,986 females)
Diagnoses with a significant difference (non-overlapping CI intervals) between IRs or MRs in GSDs and all other breeds.
D AR, dog years at risk GSD, German shepherd dog MR, mortality rates RR, relative risk

TA L 6 Diagnoses not included in the group immunological , but with proposed immune related background

	Mean age at first claim, GSD ears (95 CI)	IR, GSD morbidity Cases 10,000 D AR (95 CI)	RR, morbidity
Circumanal fistulae	6.1 (5.8 to 6.3)	25.5 (22.8 to 28.2)	46.0
PI	3.6 (3.2 to 3.9)	11.7 (9.8 to 13.5)	32.5
ypothyrosis	6.5 (6.0 to 7.0)	7.4 (5.9 to 8.9)	0.6
GSD pyoderma	5.8 (5.2 to 6.4)	7.1 (5.7 to 8.5)	336.3
Chronic superficial keratitis, pannus	6.3 (5.7 to 6.8)	6.0 (4.7 to 7.3)	16.0
Demodex	2.2 (1.6 to 2.8)	2.8 (1.9 to 3.7)	1.4
Chronic eosinophil gastritis enteritis gastroenteritis	4.0 (2.8 to 5.1)	1.7 (1.0 to 2.4)	1.5
Chronic lymphocytic plasmacytic enteritis	3.4 (1.7 to 5.1)	0.5 (0.1 to 0.9)	1.9

Ranked by incidence rate (IR)
Total number of GSDs 32,486 dogs (16,500 males and 15,986 females)
Diagnoses with a significant difference (non-overlapping CI intervals) between IRs in GSDs and all other breeds.
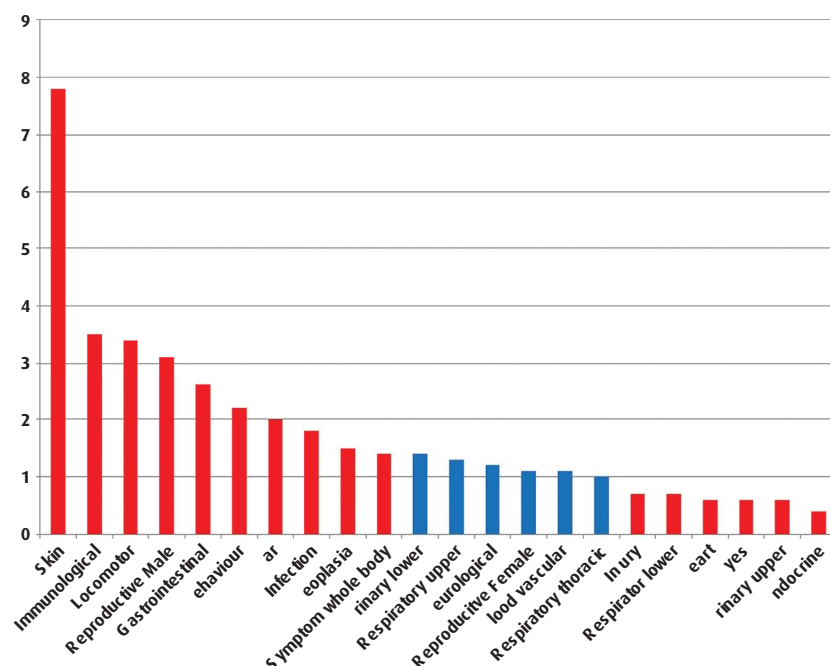D AR, dog years at risk PI, exocrine pancreatic insufficiency GSD, German shepherd dog RR, relative risk

FIG 2 Relative Risk (RR) for general causes of death in the German shepherd dog (GSD) compared with all other breeds. ((Incidence rate (IR) in breed) IR all other breeds)). Disease categories with a significant difference (non-overlapping CI intervals) between IRs in GSDs and all other breeds have red bars. ote T he distance between the RRs 0.5 and 1.0 e uals the distance between 1.0 and 2.0

Discussion

T he insurance database used for this study was developed to register claims, and it cannot be considered a perfect source of information on the disease prevalence. owever, the number of dogs in the database is large, and high statistical power can be achieved, making it well suited to describe the occurrence of disease and death within a breed and differences across breeds. Veterinarians assign diagnoses using a standardised diagnostic registry, providing a level of consistency, but their underlying accuracy is unknown. In this study, only the first veterinary claim for each animal has been included, which is most appropriate for examining and comparing risk across breeds, but underestimates the entire burden of disease, in that, individual dogs with chronic conditions might have many veterinary visits over the course of their lives. So, given that these are data from one country, and there are limitations of the insurance database, exact rates and risks should be extrapolated cautiously. otwithstanding this caution, there is clear indication of significant specific problems in GSD s compared with other breeds of dogs.

T he A gria insurance database has been validated. T he agreement between the database and original veterinary records for diagnosis was 84.0 and 84.9 per cent for health and life claims, respectively, which

was considered as fair accuracy (genvall and others 1998). T he accuracy is assumed to be similar across breeds, and the RR should, therefore, be a useful and relatively unbiased tool for detecting breed predispositions. It should be noted that some of the diagnoses, for example, itching , are clinical signs rather than an aetiology, however, these designations are typically used in clinical practice. Some categories, such as skin, are anatomical locations, whereas some others are aetiological, such as immunological. T he structure of the diagnostic registry used, and the realities of clinical practice and disease result in overlap in some dogs over time, which does not diminish the usefulness of the material. Specific diagnoses with the highest morbidity in GSD s included diagnoses such as hip dysplasia , degenerative lumbosacral stenosis , pyometra and circumanal fistulae. T hese diagnoses are relatively straightforward to diagnose. It is more complicated to diagnose, for example, atopy , and there are several alternative diagnoses to assign to the atopic dog compared with the dog with circumanal fistulae or pyometra. T he accuracy of diagnostic information may vary by veterinarian and across diagnoses, but is reasonable to assume that there is no substantial bias across breeds.

G iven the realities of veterinary practice and the recording of diagnoses in the database, dogs with a condition that presents a challeng-

TA L 7 10 most common skin-related diagnoses for euthansia or death in GSDs			
	Mean age first claim, GSD ears (95 CI)	MR, GSD Cases 10,000 D AR (95 CI)	RR
Circumanal fistulae	6.4 (6.0 to 6.7)	16.0 (13.8 to 18.3)	87.9
Itching	4.3 (3.6 to 5.0)	4.1 (3.0 to 5.3)	5.8
Chronic dermatitis of unknown origin	6.2 (5.4 to 7.1)	3.6 (2.5 to 4.7)	7.0
(GSD) pyoderma	5.7 (4.6 to 6.8)	2.6 (1.7 to 3.5)	
Deep chronic pyoderma	5.7 (4.9 to 6.5)	2.4 (1.6 to 3.3)	6.9
Chronic serous dermatitis, cutis, subcutis	4.8 (3.8 to 5.8)	1.9 (1.1 to 2.6)	5.1
Acute fistulating anal sack inflammation	5.8 (2.7 to 9.0)	1.8 (1.0 to 2.5)	35.2
Furunculosis	4.9 (3.6 to 6.2)	1.7 (0.9 to 2.4)	1.6
Chronic inflammatory condition, cutis, subcutis	7.1 (6.0 to 8.3)	1.4 (0.8 to 2.1)	5.7
Symptom of disease with no established cause, cutis, subcutis	5.9 (4.3 to 7.4)	1.4 (0.7 to 2.0)	6.1

Ranked by mortality rate (MR)
Total number of GSDs 32,486 dogs (16,500 males and 15,986 females)
 Diagnoses with a significant difference (non-overlapping CI intervals) between MRs in GSDs and all other breeds.
D AR, dog years at risk GSD, German shepherd dog RR, relative risk

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TA L 8 General causes of death or euthanasia in GSDs

	Mean age at death, GSD ears (95 CI)	MR, GSD Deaths 10,000 D AR (95 CI)
Locomotor	4.6 (4.4 to 4.8)	117.6 (111.5 to 123.8)
eoplasia	7.9 (7.8 to 8.1)	73.9 (69.0 to 78.8)
Gastrointestinal	5.0 (4.8 to 5.3)	50.2 (46.1 to 54.2)
Skin	5.6 (5.6 to 6.1)	43.3 (39.6 47.1)
In ury	3.7 (3.4 to 4.0)	32.3 (29.1 to 35.6)
eurological	6.2 (5.8 to 6.6)	20.5 (17.9 to 23.1)
Immunological	4.5 (4.1 to 4.9)	15.9 (13.6 to 18.1)
eart	6.0 (5.4 to 6.6)	11.7 (9.7 to 13.6)
Symptom whole body	6.8 (6.3 to 7.3)	11.3 (9.4 to 13.2)
ehaviour	3.9 (3.4 to 4.4)	7.4 (5.9 to 9.0)
rinary upper	5.9 (5.2 to 6.6)	6.1 (4.7 to 7.5)
Reproductive female	8.1 (7.5 to 8.6)	5.6 (4.2 to 6.9)
lood vascular	5.7 (4.9 to 6.5)	4.6 (3.3 to 5.8)
Infection	5.5 (4.6 to 6.4)	3.8 (2.7 to 4.9)
ndocrine	6.8 (6.0 to 7.6)	3.6 (2.5 to 4.7)
rinary lower	6.7 (5.8 to 7.6)	3.0 (2.0 to 4.0)
Respiratory lower	6.3 (5.1 to 7.5)	2.6 (1.7 to 3.5)
ar	6.8 (5.9 to 7.7)	2.5 (1.6 to 3.4)
Reproductive male	7.7 (6.9 to 8.5)	2.2 (1.4 to 3.0)
yes	7.1 (6.2 to 8.0)	2.1 (1.3 to 2.9)
Respiratory upper	6.4 (5.3 to 7.4)	1.9 (1.1 to 2.7)
Respiratory thoracic	7.2 (5.8 to 8.7)	0.9 (0.4 to 1.5)

Ranked by mortality rate (MR)
Total number of GSDs 32,486 dogs (16,500 males and 15,986 females)
D AR, dog years at risk GSD, German shepherd dog

gastroenteritis as immune-related. A lso, a dog may be given multiple different diagnoses over the course of a chronic problem, and show up in different categories. In order to handle the diagnostic considerations described in this paragraph, we used hierarchical classifications and presented both general and specific diagnostic categories. nly one event per dog was counted, regardless of how many times the dog was seen for conditions within a general category. e can then assume, for example, that the rate for a specific diagnosis represents the more conservative estimate, and that for the more general category contains all dogs which had some form of that or related conditions. A nother benefit to the approach used here is that every thing is compared with all other breeds, and several conditions and categories clearly occur at an increased rate in G SD s.

M orbidity was defined as claims for veterinary care that exceeded the deductible cost and did not include any low-cost events or conditions suffered by the dog when it was initially insured. As a result, few low-cost diagnoses or treatments were recorded. Furthermore, when investigating the mean age at first claim, it must be remembered that this is not the age of the first sign of a disease. For some diseases, it takes months of investigations before diagnosis can be set.

M ortality rate within a breed is affected by various factors, including the function of the dog s and the owner s attitudes. reeds kept solely as companion animals may have owners who are more prone to provide the animals with veterinary treatment for a longer time within their financial capacity. y contrast, breeds used in service are more dependent upon usefulness which could result in euthanasia if the dog s work is affected by the disease, resulting in higher M R.

owever, G SD s in Sweden are used both as companion and working dogs. G SD s insured in A gria should be considered representative for the average dog in A gria in regard to the distribution of companion and working dogs, making it relevant to compare mortality in G SD s with other breeds. ne limitation of the mortality data is the limitation to dogs less than 10 years old, yielding an underestimation of the total mortality rate in disorders affecting old animals. owever, presumably, illness and death in the first 10 years of life would be those we would be most interested in preventing.

Skin-related disorders were the most common cause of veterinary care events for a G SD . Itching , was the specific dermatological code with highest incidence rate in which the G SD is also slightly over-represented compared with other breeds. M any of the dogs in the itching group were also represented in the group of allergic diagnoses indicating that the allergic dog was diagnosed with itching before an investigation for allergic disease was completed (data not shown). M ale dogs were over-represented in infectious inflammatory skin disorders, such as acute dermatitis, hot spot and the G SD pyoderma. A predisposition to the GSD pyoderma in male dogs has earlier been

ing (or expensive) diagnostic problem are likely to be hidden within various diagnostic codes. T his would suggest that cases would be missed and the actual rate of a condition underestimated if only the rate based solely on the specific diagnosis was examined. For example, some truly atopic dogs could have been diagnosed simply with itching . Indeed, an atopic dog could have been assigned various diagnoses, such as symptoms of allergic disease , itching , allergy with skin affection or atopy . C onversely, it is possible that veterinarians might assign the code atopy , in spite of the diagnostic criteria re uirements for that condition not being met, but it is likely that misclassification in this direction is less. T he recorded diagnosis of atopy in the insurance database has been validated against practice records and the agreement was considered acceptable (dtvedt and others 2006a, b). Similarly for other immune-related diagnoses, we are hampered by not knowing refinement of the diagnostic process. For example, gastroenteritis could have an immune-related background, but confirmation of that determination re uires profound diagnostic procedures, and it is, of course, incorrect to classify all general diagnoses of

TA L 9 15 most common diagnoses for euthanasia or death in GSDs

	Mean age at death, GSD ears (95 CI)	MR, GSD Cases 10,000 D AR (95 CI)	RR
ip oint dysplasia	2.7 (2.5 to 2.9)	43.8 (40.1 to 47.6)	8.0
Circumanal fistulae	6.4 (6.0 to 6.7)	16.0 (13.8 to 18.3)	87.9
Degenerative lumbosacral stenosis	7.0 (6.7 to 7.4)	16.0 (13.8 to 18.3)	12.9
Traffic in ury	3.2 (2.8 to 3.6)	14.5 (12.4 to 16.7)	0.7
xocrine pancreatic insufficiency	3.9 (3.5 to 4.3)	13.7 (11.6 to 15.8)	44.4
Mammary tumour	8.8 (8.6 to 9.0)	11.3 (9.4 to 13.2)	2.6
Atopy	4.3 (3.9 to 4.8)	7.9 (6.3 to 9.5)	7.3
Chronic deformative arthrosis in the elbow oint	4.8 (4.1 to 5.5)	7.9 (6.3 to 9.5)	3.5
Leukaemia malignant lymphoma	6.2 (5.6 to 6.7)	6.3 (4.9 to 7.8)	1.3
Lymphoma of the spleen	8.8 (8.6 to 9.1)	5.5 (4.2 to 6.8)	4.2
Spondylosis	8.0 (7.6 to 8.5)	5.4 (4.1 to 6.7)	5.5
Torsion of stomach	6.8 (6.1 to 7.5)	5.4 (4.1 to 6.7)	3.1
Idiopathic epilepsy	4.8 (4.2 to 5.5)	5.3 (4.0 to 6.6)	0.7
Change in behaviour	3.8 (3.1 to 4.4)	4.9 (3.6 to 6.2)	2.3
Pyometra	8.1 (7.6 to 8.7)	4.8 (3.6 to 6.1)	1.1

Ranked by mortality rate (MR)
Total number of GSDs 32,486 dogs (16,500 males and 15,986 females)
Diagnoses with a significant difference (non-overlapping CI intervals) between MRs in GSDs and all other breeds.
D AR, dog years at risk GSD, German shepherd dog RR, relative risk

shown in case studies (Denerolle and others 1998) indicating that males are predisposed to infectious skin disease. ot surprisingly, the GSD pyoderma was a diagnosis seen almost exclusively in GSDs.

There was a strong predisposition for immune-related diseases in GSDs. The ma ority of these cases were allergy. The mean age at first claim was lower for GSDs diagnosed with an allergic diagnosis, compared with GSDs with autoimmune diagnoses, which appeared slightly later. The autoimmune disorder lupus was more common in males, which is in agreement with a study of lupus in dogs from 1996 (ansson and others 1996). ther studies have reported different gender influence in various canine autoimmune diseases (Dodds 1977, Reimer and others 1999, alch and Mackin 2007, ansson- amlin and Lill ehook 2009). In human lupus, women are reported to be predisposed (Doukas and others 2013). The autoimmune disorders were fairly uncommon, however, and any further conclusions regarding age and sex distributions are, therefore, unreliable.

Although skin problems are common morbidities among dogs in general, and certain breeds are at increased risk, the GSD stands out as a breed in which the problems are severe enough to result in euthanasia. Looking at specific diagnoses causing death within the skin group, circumanal fistulae was over-represented. This is a disorder with a proposed immune-related aetiology (Day and eaver 1992). It was the skin-related diagnosis with the highest mortality rate in GSDs. Another disorder with a suspected immune-related background, but not included in the general category immunological , is PI, or the more specific diagnosis, exocrine pancreas atrophy. This is a disease mainly seen in a few breeds, including GSDs, and according to the mortality data, it is a diagnosis often resulting in euthanasia, being the fifth most common cause of death in GSDs. The disease was diagnosed in young middle-aged dogs, and the affected dogs were euthanased at an average age of 3.9 years, which is young compared with other causes of death euthanasia.

Locomotor disorders were the most common causes of euthanasia in GSDs, and hip oint dysplasia was the specific diagnosis with the highest mortality, followed by degenerative lumbosacral stenosis. ip oint dysplasia is a disorder causing euthanasia in relatively young animals, while older animals are euthanased due to degenerative lumbosacral stenosis.

GSDs did have a lower risk for heart disease as well as endocrine disorders, both regarding morbidity and mortality, compared with all breeds (data not shown). Many of these conditions manifest at older ages, and the fact that the GSD has a relative lower survival than many breeds, could to some extent explain the under-representation of GSDs within this group of disorders.

Morbidity and mortality data in this study have both verified previous indications of the pattern of diseases in GSDs and new insights in ma or health problems within the breed. GSDs had a higher morbidity due to immune-related diseases compared with other breeds, which is in agreement with other epidemiological studies and case studies showing a predisposition for these disorders in GSDs (isselink and others 1985, Day and others 1986, att and others 1991, Day and eaver 1992, Clark and others 2005, dtvedt and others 2006a, b). This predisposition is suggested to be a result of inherited defects in the immune system (hitbread and others 1984, Day and Penhale 1988, att and others 1991, Griot- enk and others 1999). A predisposition for low serum IgA levels have earlier been reported in GSDs (hitbread and others 1984). Recently, genome-wide analysis in GSDs reveals associations of a locus on CFA 27 with atopic dermatitis. aplotype association analysis from the fine-mapping data indicated association to the gene, plakophilin 2 (P P2), known to be important for skin structure. Low (er) IgA levels were in that study correlated to increased risk for atopy (Tengvall and others, 2013). Features of skin structure, as well as immunological parameters as IgA in GSDs, might well also influence the high prevalence of pyodermas, dermatitis and circumanal fistulae, thereby explaining a fair share of the specific pattern of disease in GSDs. An evaluation of these features, as well as effects on it by preventive interventions, will be further explored in subse uent studies. More than 50 per cent of all GSDs used for breeding in Sweden have sires from other countries (mainly urope) S C 2011, indicating that the Swedish population of GSDs is genetically representative for the uropean GSD population. The

results of this study, thereby, are suggested to be relevant for Sweden and also urope, and possibly beyond.

In conclusion, we describe a breed-specific pattern of diseases in GSDs and can confirm that the GSD is predisposed to immune-related disorders such as allergies, circumanal fistulae and exocrine pancreas atrophy. These disorders are common causes of both morbidity and mortality in GSDs. Further research should be focused on investigating the immune function in GSDs and also the predisposition to skin disorders, especially in male GSDs.

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