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Prevalence, survival analysis and multimorbidity of chronic diseases in the general veterinarian-attended horse population of the UK

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ABSTRACT

The average age of the global human population is increasing, leading to increased interest in the effects of chronic disease and multimorbidity on health resources and patient welfare. It has been posited that the average age of the general veterinarian-attended horse population of the UK is also increasing, and therefore it could be assumed that chronic diseases and multimorbidity would pose an increasing risk here also. However, evidence for this trend in ageing is very limited, and the current prevalence of many chronic diseases, and of multimorbidity, is unknown. Using text mining of first-opinion electronic medical records from seven veterinary practices around the UK, Kaplan-Meier and Cox proportional hazard modelling, we were able to estimate the apparent prevalence among veterinarian-attended horses of nine chronic diseases, and to assess their relative effects on median life expectancy following diagnosis. With these methods we found evidence of increasing population age. Multimorbidity affected 1.2% of the study population, and had a significant effect upon survival times, with co-occurrence of two diseases, and three or more diseases, leading to 6.6 and 21.3 times the hazard ratio compared to no chronic disease, respectively. Laminitis was involved in 74% of cases of multimorbidity. The population of horses attended by UK veterinarians appears to be aging, and chronic diseases and their co-occurrence are common features, and as such warrant further investigation.

1. Introduction

The non-racing, mixed breed horse population of the UK has been relatively neglected to date in terms of research into disease burden and population structure (Mellor et al., 1999; Hotchkiss et al., 2007; Ireland et al., 2013; Wylie et al., 2013). There may be as many as one million horses in the UK, yet little is known about the health and longevity of the vast majority (British Equestrian Trade Association, 2011). Reasons for this include the lack of a central database of mandatory horse passport details since withdrawal of funding from the National Equine Database in 2012, and the fragmented nature of first-opinion equine veterinary services (Boden et al., 2013). Collation of health and disease data occurs on a small scale periodically, but relies upon either owner-reporting of health problems or voluntary submission of laboratory samples, which, although informative and helpful, are both subject to significant bias if results were to be extrapolated to the general equine population (Slater, 2014; Animal Health Trust (AHT) et al., 2015). Chronic or recurrent disease is undoubtedly a feature of this population, but the extent to which it affects longevity and welfare is unknown.

Multimorbidity is defined as the co-occurrence of multiple disease conditions within an individual without reference to an index condition (Islam et al., 2014). The study of multimorbidity in medical research is currently popular, as recognition of the greater strain multimorbidity places upon health services, and its detrimental effect on patient welfare and longevity are growing (Islam et al., 2014; Pache et al., 2015). Understanding multimorbidity patterns can help uncover commonalities in aetiology or risk factors between previously unlinked conditions, and could improve patient care by shifting treatment emphasis from individual diseases to co-occurring groups of disease, especially where treatment regimens for co-occurring diseases are discordant. The average human lifespan in the UK continues to rise, and with it, the proportion of people living with multiple chronic diseases (Pache et al., 2015; Wohland et al., 2015). It has been often cited that the average age of horses in the UK is also increasing, but this assumption is based upon limited studies, and methodologies less robust than those used by UK human health authorities (Brosnahan and Paradis, 2003).

This study aimed to use first-opinion medical records to quantify the burden of a number of common chronic diseases within

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a sample of the general veterinary-attended horse population in the UK, and to estimate their effects upon survival. The apparent prevalence of comorbidity (co-occurrence of two diseases) and multimorbidity (co-occurrence of more than two diseases) were also sought, as were the effects of co- and multimorbid states on survival. A secondary aim was to implement demographic methodologies to ascertain whether the population under study was ageing over time, as has been previously postulated. These results will constitute the first such analyses on this large and diverse population, and will serve as benchmarks for future studies of the effects of chronic disease and multimorbidity in horses.

2. Materials and methods

2.1. Data

Free-text first-opinion equine medical records spanning twenty-six years (1987–2013) were collected from a convenience sample of seven first opinion equine veterinary practices around the UK, and reformatted into comma-separated values format (n = 1001375 records). Records included the following database; unique numerical identification number, date of entry into the system (date of record), sex, date of birth, breed, practice, and a field containing free-text medical records with prescription information. Records missing the date of birth or record entry were excluded, as were records of non-equine consultations, and records entered after 2012. Sex was converted into four categories; unknown, female, male, neutered male. Breed was converted into the following groups; Arab/Arab cross, Cob/Cob cross, Draught/Draught cross, Native/Native cross, pony/pony cross, Thoroughbred/Thoroughbred cross, Warmblood/Warmblood cross, Welsh/Welsh cross, other and unknown. Descriptions of each veterinary practice are contained in Table 1. All data cleaning was conducted in R statistical environment (R Core Development Team, 2015).

2.2. Text mining

Nine chronic (or recurrent) conditions were chosen for study *a priori*, after discussion with experienced equine clinicians; neoplasia, pituitary pars intermedia dysfunction (PPID), equine metabolic syndrome (EMS), grass sickness, laminitis, navicular syndrome, osteoarthritis, recurrent airway obstruction (RAO), and sarcoids. These were chosen as diseases that can be diagnosed in first opinion practice, which are chronic or recurrent in nature and are commonly incurable. They were also considered to have names that would be unlikely to appear in medical records unless the animal in question was thought to be suffering from them. Commercially available text mining software (WordStat v7.0, Provalis Research Inc.) was used to construct dictionaries that would allow identification of records where each disease was mentioned, in an iterative process modified from the approach detailed by Lam et al. (Lam et al., 2007) and validated by Anholt et al. (2014). 'Diagnosis' of disease in this context was defined as inclusion of these key words or phrases, without requirement of additional information such as test results. 'Diagnoses' were therefore reflective of the thought process and professional opinion of the veterinarian regarding the case at hand, as opposed to an accurate and verbose description of the diagnostic criteria of the case (which were commonly missing). Additionally, a dictionary was constructed to identify records of death (natural or euthanasia) (see Appendix A). These criteria were chosen in order to identify the real-world decisions (e.g. euthanasia) taken following delivery of a veterinarian's clinical judgement in each case. Dictionary construction was performed on the full dataset to maximise coverage, and negations were added to a list of excluded words and phrases as necessary. Internal validation was conducted through manually checking the 'keyword-in-context' output for each disease; and altering the dictionary and/or excluded words list as necessary. Data were subsequently exported with one column per disease (containing binary data indicating presence/absence of disease) in place of free text records; plus a binary column indicating presence/absence of death at each record.

2.3. Life expectancy following initial veterinary care episode

Period life tables were constructed for three-year periods near the beginning and end of the study (1995–1997, and 2010–2012), for records from five practices (two practices were excluded due to significantly lower ages at the time of death [Practice 4], and high annual proportion of deaths [Practice 7]). Life expectancy (following first recorded veterinary episode) with 95% confidence intervals was calculated (Chiang, 1968, 1978).

2.4. Univariable and multivariable modelling of chronic diseases

Survival analyses were conducted using R packages 'survMisc' and 'survival' (Dardis, 2015; Therneau, 2015). For each horse that had at least one record of chronic disease, the time from diagnosis to its last record in the data was computed, and the presence of a record of death was recorded as 0/1. Similarly, for those horses that were not diagnosed with any of the selected diseases, the time from their first entry in the data, to their last, was computed, and whether they were recorded as having died was noted. Kaplan-Meier survival analysis was performed to estimate median survival time following diagnosis, or following entry into the dataset (in the case of no chronic disease). Univariable Cox proportional hazard models were constructed to assess the significance of the effect of disease, sex, breed, practice, and age at the time of diagnosis (years) upon survival. Variables were retained for potential inclusion in the multivariable model if the p-value <0.25, and the likelihood ratio test (LRT) p-value compared with the null model was <0.05. Categorical variables were re-grouped based on similarity of exponentiated coefficients and Wald significance, as required. A forward stepwise manual model building procedure was implemented, with significant variables included in order of highest to lowest log-likelihood (Dohoo, 2009). Variables were retained in the multivariable model if LRT p-value <0.05. All pairwise interactions between retained variables were investigated for significance and their effect on existing coefficients. Proportional hazards assump-

Table 1
Descriptive details of a convenience sample of seven first-opinion veterinary practices serving horses, that contributed data to the current study.

Practice	Number of veterinarians	Location	Provide own out-of-hours	RCVS Accredited	Species covered	Number of branches
1	11	Scotland	Yes	Yes	Mixed	2
2	21	Central England	Yes	Yes	Equine	1
3	17	Northern England	Yes	Yes	Mixed	5
4	14	Central England	Yes	No	Mixed	4
5	11	Southern England	Yes	No	Equine	1
6	4	Northern England	Yes	Yes	Large	1
7	8	Northern England	Yes	No	Mixed	2

RCVS Royal College of Veterinary Surgeons.

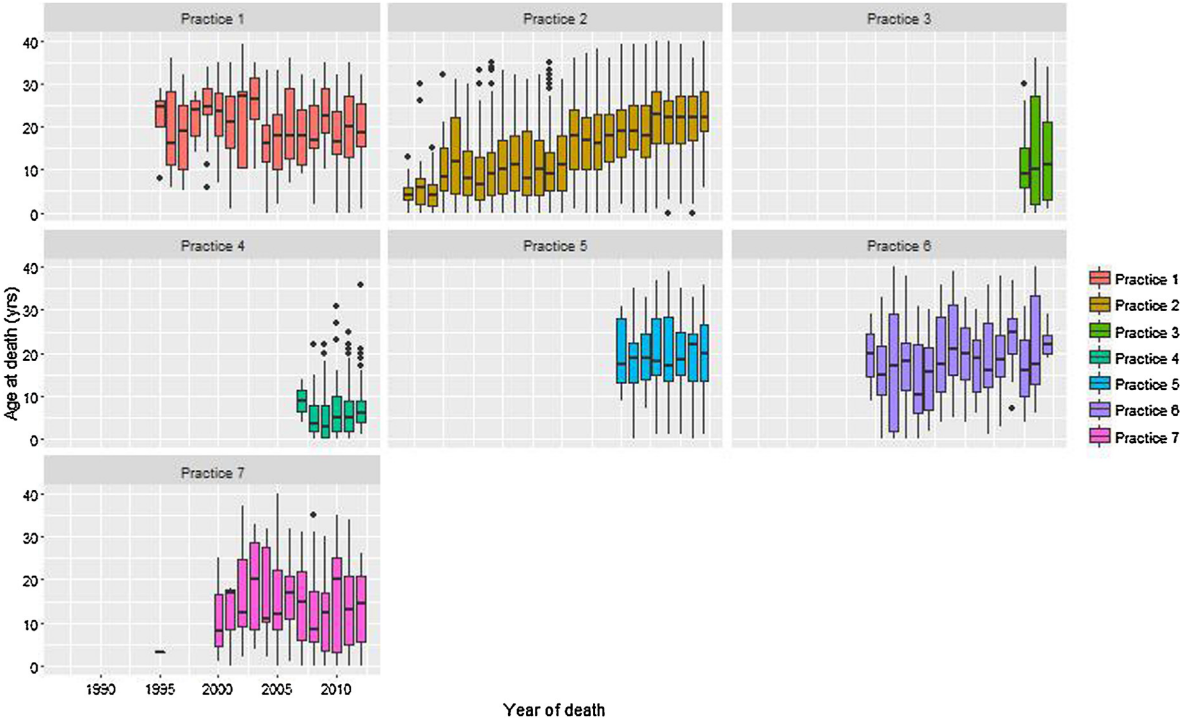

Fig. 1. Distributions of age (years) at the time of death of horses seen at a convenience sample of UK first-opinion veterinary practices between 1987 and 2013.

tions of the model globally, and of each variable individually (all levels of categorical variables assessed *en masse* and individually) were assessed by visual inspection of scaled Schoenfeld residuals (Therneau and Grambsch, 2000; Therneau, 2015). The influence of individual observations was assessed by visual inspection of delta-betas for continuous predictors (Therneau and Grambsch, 2000).

2.5. Modelling multimorbidity

For the purposes of this study, 'comorbid' indicates a horse diagnosed with two chronic diseases, and 'multimorbid' indicates a horse diagnosed with more than two diseases. The association of disease co-occurrence with survival was analysed after computing the time from commencement of the lifetime disease co-occurrence state (i.e. 'comorbid' horses: date of diagnosis of the second disease, 'multimorbid' horses: date of diagnosis of the third disease) to the date of the last entry for that horse, with 'no chronic disease' as the referent level. Model building proceeded similarly to disease modelling above. Independent variables screened for their association with survival included lifetime disease co-occurrence status (none, one, two, or more than two chronic diseases), age at time of diagnosis (years), practice, breed and sex. Again, breeds were grouped according to similarity of exponentiated hazard ratio and Wald significance. Kaplan-Meier survival analysis was conducted and probability of survival plotted.

Ethical approval for this study was granted by the Research Ethics Committee, School of Veterinary Medicine, University of Glasgow.

3. Results

3.1. Demographic characteristics

The cleaned dataset contained 515807 records from 70477 horses, of which 12796 (18%) were male, 25214 (36%) were neutered males, 26018 (37%) were female, and 6487 (9%) were of unknown sex. Seven practices contributed to the dataset. The annual age at the time of death for horses in each practice is shown in Fig. 1, and the proportion of horses that died annually is shown in Fig. 2. Overall, the mean age at death for all horses was 16.5 years (median 17, IQR 8–24 years).

Table 2
Summary of the age (years) at the time of diagnosis for a selection of chronic diseases recorded in a UK database of electronic medical records from the general horse population between 1987 and 2013.

Disease	Minimum	Q1	Median	Q3	Maximum
No chronic disease	0	3	6	12	40
Osteoarthritis	0	7	14	21	39
Laminitis	0	8	15	22	40
PPID	0	15	21	26	40
EMS	1	15	21	28	38
Grass Sickness	0	5	9	15.5	34
Navicular Syndrome	0	6	10	16.5	36
Neoplasia	0	7	14	22	40
RAO	0	6	13	21	39
Sarcoids	0	6	11	19	40

Q1 25th percentile; Q3 75th percentile.

3.2. Quantification of disease burden

In total, 9013 horses (12.8%) had at least one chronic disease (maximum of 6) over the course of the study. The number of records in which each disease was noted, and the number of horses those records pertain to (in brackets), was as follows; neoplasia 1159 records (978 horses), PPID 3199 (2011), EMS 154 (140), grass sickness 72 (66), laminitis 6110 (4082), navicular syndrome 67 (60), osteoarthritis 1281 (1171), RAO 1388 (1232), sarcoids 3476 (2070). Death was recorded for a total of 4689 (6.7%) horses over the study period.

A summary of the age at the time of diagnosis for each disease is shown in Table 2.

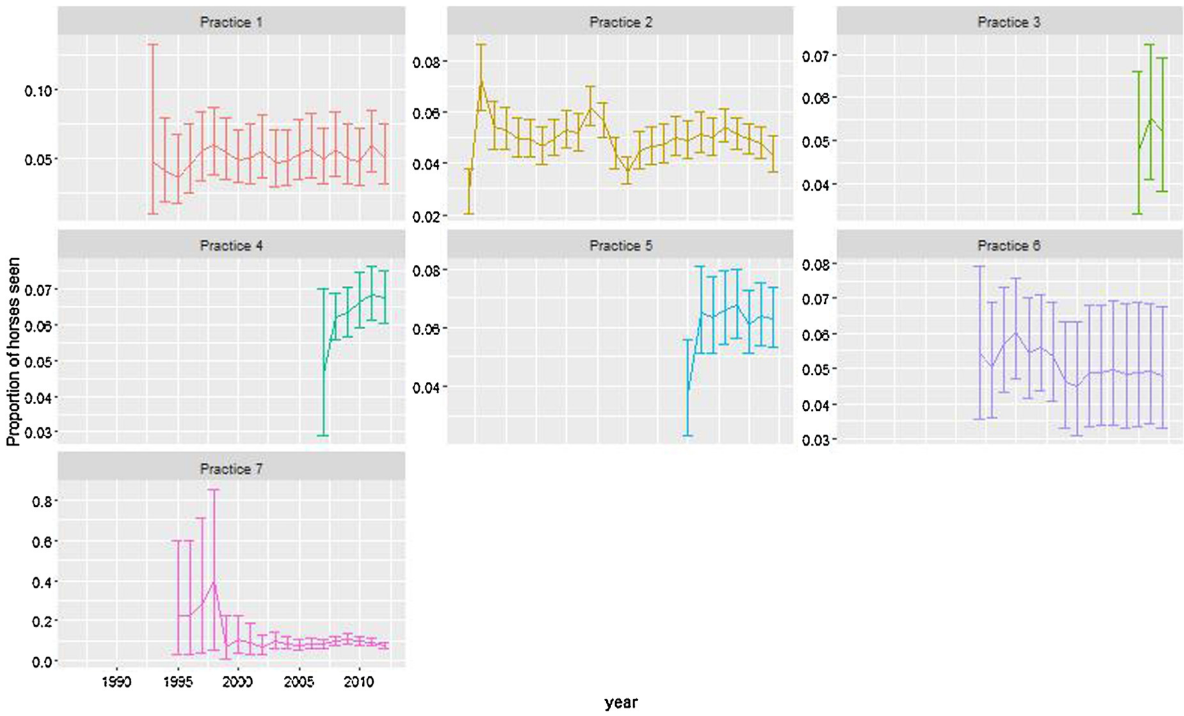

Fig. 2. Proportion of veterinary-attended horses seen at a convenience sample of first-opinion UK equine veterinary practices that died or were euthanased per practice per year between 1987 and 2013.

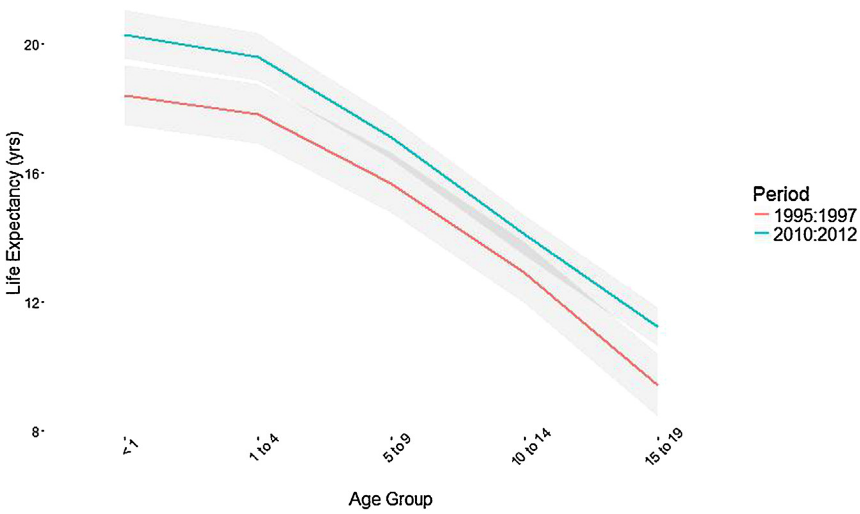

Fig. 3. Life expectancy (years) following first recorded veterinary care episode of horses born in 1995–1997, versus those born in 2010–2012, for different age groups. Grey bands indicate 95% confidence intervals. Practice 4 and Practice 7 were excluded from these analyses due to significant differences in demography.

3.3. *Life expectancy following first veterinary care episode*

Life expectancy following first veterinary care episode for horses born in 1995–1997 and 2010–2012, separated by age group, is shown in Fig. 3. Horses born in the later time period were found to have a longer life expectancy at birth than those born in the earlier time period.

3.4. *Multimorbidity prevalence*

In total, 2125 horses were diagnosed with more than one chronic disease (3.0% of the total population; 23.6% of those with at least one chronic condition). Of these, 1582 had two diseases, 406 had three diseases, 120 had four diseases, 16 had five diseases, and 1 had six diseases. Information on the number of horses experiencing each combination of at least two co-occurring diseases is contained in Table 3. Laminitis was a feature of 74% of horses with multiple diseases, and PPID was a feature in 49%.

3.5. *Survival analyses*

The final multivariable model contained the following significant variables; disease, age at diagnosis (years), breed, and practice (included as a random effect). Kaplan-Meier plots of survival following diagnosis of each disease, and for horses without chronic disease, are shown in Fig. 4. Median survival times estimated from this model, alongside results of Cox proportional hazard modelling are shown in Tables 4 and 5. The assumption of proportionality

Table 3
Co-occurrence matrix of a selection of chronic diseases in a UK general veterinary-attended horse population, identified through text mining electronic medical records from seven first-opinion practices between 1987 and 2013. Numbers on the diagonal are the number (%) of horses diagnosed with that disease in the data (n = 70477).

	Osteoarthritis	Navicular syndrome	Neoplasia	PPID	EMS	Grass Sickness	Laminitis	RAO	Sarcoids
Osteoarthritis	1171 (1.7)								
Navicular syndrome	3	60 (0.1)							
Neoplasia	65	0	978 (1.4)						
PPID	132	3	124	2011 (2.9)					
EMS	14	0	13	86	140 (0.2)				
Grass Sickness	1	0	3	8	1	66 (0.1)			
Laminitis	304	11	235	806	103	9	4082 (5.8)		
RAO	79	6	68	136	10	4	321	1232 (1.7)	
Sarcoids	121	4	166	256	23	3	408	148	2070 (2.9)

EMS Equine Metabolic Syndrome; PPID Pituitary Pars Intermedia Dysfunction; RAO Recurrent Airway Obstruction.

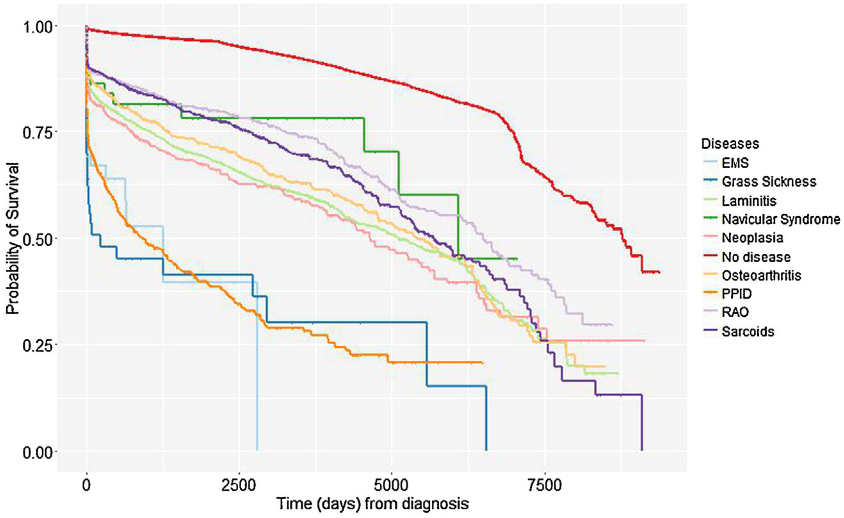

Fig. 4. Kaplan-Meier survival plot of a selection of chronic diseases found to significantly affect the probability of survival in a UK veterinary-attended general horse cohort.

Table 4
Results of multivariable Cox proportional hazard models of nine chronic diseases diagnosed in a convenience sample of first-opinion equine veterinary practices between 1987 and 2013, as detected through text mining of electronic medical records.

		Number of horses	HR (SE)	Wald *p*-value	HR 95% CI
Disease	No chronic disease	61464	1 (REF)		
	Neoplasia	978	6.52 (0.07)	<0.01	5.72–7.44
	PPID	2011	9.27 (0.05)	<0.01	8.37–10.27
	EMS	140	9.61 (0.17)	<0.01	6.85–13.47
	Grass Sickness	66	18.74 (0.18)	<0.01	13.25–26.50
	Laminitis	4082	5.94 (0.04)	<0.01	5.49–6.42
	Navicular syndrome	60	5.19 (0.29)	<0.01	5.72–7.44
	Osteoarthritis	1171	5.08 (0.07)	<0.01	4.47–5.77
	RAO	1232	4.51 (0.07)	<0.01	3.95–5.15
	Sarcoids	2070	4.91 (0.06)	<0.01	4.39–5.49
Age at diagnosis (years)			1.10 (0.02)	<0.01	1.09–1.10
Breed Group	Other/unknown	67680	1 (REF)		
	Arab	988	0.88 (0.12)	0.28	0.70–1.11
	Pony/Welsh	4632	0.79 (0.06)	<0.01	0.70–0.79

HR: Hazard Ratio, 95% CI: 95% confidence interval, SE: standard error, REF: referent category.

of hazards, as assessed using plots of scaled Schoenfeld residuals, was upheld for each variable. No observations were found to exert undue influence on the model.

The results of Cox proportional hazard modelling of lifetime disease co-occurrence status (with no chronic disease as the referent level, n = 61464) are contained in Table 6.

Survival curves of lifetime disease co-occurrence status are shown in Fig. 5.

The proportion of horses diagnosed with two or more chronic diseases (multimorbid status) over time is shown in Fig. 6. This proportion was 0.5% in 1995–1997, and 1.3% in 2010–2012.

4. Discussion

This study is the first to report estimates of median life-expectancy and hazard ratios following diagnosis of a number of

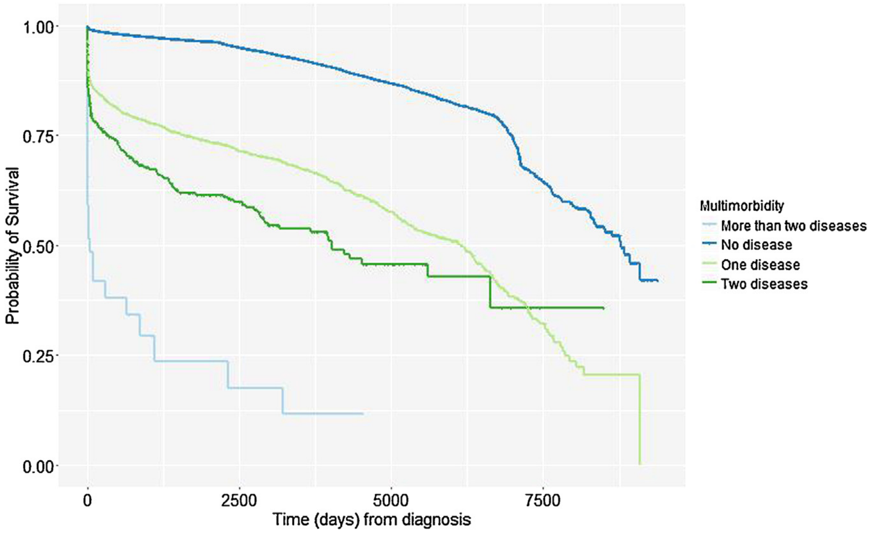

Fig. 5. Kaplan-Meier survival plot of lifetime disease co-occurrence status (considering a selection of nine chronic diseases) of a horses seen at a convenience sample of UK first-opinion equine veterinary practices between 1987 and 2013.

Table 5
Median life expectancy following diagnosis (other independent variables held at their reference or median levels) of a selection of chronic diseases in a convenience sample of the general veterinary-attended horse population of the UK between 1987 and 2013.

Diagnosis	Median life expectancy in years following diagnosis (95% CI)	Median (IQR) age at diagnosis (years)
No chronic disease	22.7 (21.9–NA)	6 (3–12)
Neoplasia	12.3 (11.4–13.6)	14 (7–22)
PPID	9.8 (9.0–10.7)	21 (15–26)
EMS	9.0 (7.0–12.4)	21 (15–28)
Grass Sickness	4.0 (2.3–6.8)	9 (5–15.5)
Laminitis	13.4 (12.7–14.3)	15 (8–22)
Navicular syndrome	14.4 (10.5–19.5)	10 (6–16.5)
Osteoarthritis	14.5 (13.3–15.9)	14 (7–21)
RAO	16.4 (15.0–17.9)	13 (6–21)
Sarcoids	15.4 (14.3–16.7)	11 (6–19)

CI confidence interval; NA estimate not available.
IQR Inter-quartile Range; EMS Equine Metabolic Syndrome; PPID Pituitary Pars Intermedia Dysfunction; RAO Recurrent Airway Obstruction.

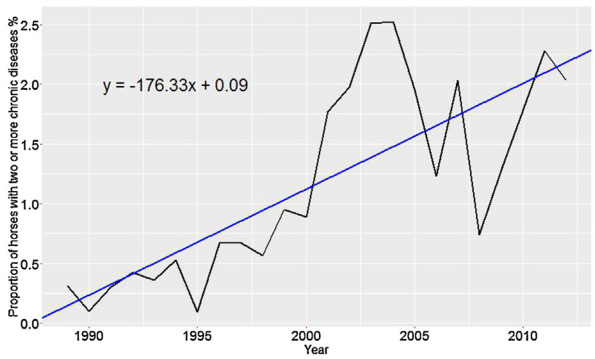

Fig. 6. Annual proportion of horses seen at a convenience sample of UK first-opinion veterinary practices that were diagnosed with more than two of the nine specified chronic diseases over the study period (1987–2013).

Table 6
Results of multivariable Cox proportional hazard models of co- and multimorbidity of nine chronic diseases in a database of electronic medical records from a convenience sample of seven UK equine veterinary practices between 1987 and 2013.

		Number of horses	HR (SE)	*p*-value	HR 95% CI
Lifetime disease co-occurrence status	No chronic disease	61464	1 (REF)		
	One chronic disease	8201	3.06 (0.06)	< 0.01	2.70–3.47
	Two chronic diseases	743	6.61 (0.17)	< 0.01	4.70–9.31
	More than two chronic diseases	78	21.29 (0.49)	< 0.01	8.13–55.77
Age at diagnosis (years)			1.08 (0.01)	<0.01	1.06–1.09
Practice	1	2889	1 (REF)		
	2	38704	0.54 (0.15)	<0.01	0.40–0.73
	3	1442	2.57 (0.24)	<0.01	1.60–4.11
	4	14339	2.22 (0.17)	<0.01	1.58–3.11
	5	5565	0.57 (0.20)	<0.01	0.38–0.85
	6	5052	0.83 (0.20)	0.35	0.57–1.22
	7	2485	1.93 (0.20)	<0.01	1.32–2.83
Age at diagnosis*Lifetime disease co-occurrence status				<0.01*	
Age at diagnosis*Practice				<0.01*	

HR: Hazard Ratio, 95% CI: 95% confidence interval, SE: standard error, REF: referent category.
* LRT *p*-values for model with interaction versus model without.

chronic diseases in the veterinarian-attended general horse population of the UK. Over 12% of the horses in this study were diagnosed with at least one of nine chronic diseases, and 1.2% of horses were diagnosed with more than one chronic disease.

Not all horses in the UK are registered with a veterinarian, and of those that are, a proportion do not receive veterinary products or attention, therefore using electronic medical records to ascertain the prevalence of disease or demographic information is liable to a degree of selection bias. The results reported here cannot, therefore, be directly extrapolated to the wider veterinary-attended population of horses. Similarly, due to the convenience nature of the sampling of veterinary practices carried out, the results presented may not be fully generalizable to the general veterinary-attended horse population of the UK. Currently in veterinary medicine in the UK, no systematic fixed vocabulary exists for the recording of medical events, so clinical signs, differential diagnoses, tests and treatments are all recorded using free-text entries. Variability in spelling, nomenclature and phraseology lead to a plethora of ways in which disease is documented. The iterative nature of the text-mining process, where included words or phrases are internally validated through inspection of their appropriateness in context, has been shown to lead to acceptable levels of sensitivity and specificity compared with manual classification (Anholt et al., 2014). Categorisation errors are unavoidable with any form of automated text-mining, and this must be borne in mind with regards to the results presented here, especially where nomenclature necessarily overlaps between related diseases (e.g. sarcoids, PPID and other neoplasias). Additionally, owners are free to register their animal with any number of veterinary practices, and to move practices at any time. Therefore, the records used in this study may not represent the entirety of that animal's medical history, and duplication (where a horse received medical attention at more than one of the practices used in the study) may have occurred, although this could be assumed to be rare. In addition, dictionary terms were chosen to optimise specificity of case identification, with some unavoidable reduction in sensitivity, in order to be sure of the diagnoses assigned, thus disease 'prevalence' reported here may be less than reported in other studies, for some diseases. There was potential for a degree of overlap in the dictionaries used to identify cases of sarcoids and non-sarcoid neoplasia, however the terms were retained due to the strong suspicion amongst the authors that these would be accurately differentiated in most cases by veterinarians, due to the prevalence and characteristic nature of sarcoids.

The group of diseases studied in these analyses represent a small number of chronic/incurable conditions in equine medicine, but they bear certain similarities in terms of nomenclature. Inclusion of the disease name (or a derivation of it) in an animal's medical records was considered to be very likely to indicate that the veterinarian entering the record was strongly suspicious of, or had diagnosed, that condition. This is unlike conditions such as dental disease, chronic lameness or recurrent colic, whose terminology is variable, and could relate to a spectrum of disease including curable conditions. This supposition was borne out though examination of the final dictionary terms in context. Given the length of time over which these data were collected, historic terminologies for the conditions studied were also included, e.g. chronic obstructive pulmonary disease or heaves. Grass sickness is very rarely encountered in its true chronic form, but was included here (all forms thereof) because it represented a disease with a well-recognised high mortality rate and short disease course. Grass sickness thereby acted as a form of positive control, and allowed comparison with conditions of lower mortality and more protracted disease courses. Neoplasia constitutes a large number of different diagnoses in equine medicine, which may be reached following a plethora of diagnostic tests. This group was not subdivided into specific tumour types due to small sample sizes, but also because the level of diagnostic accuracy reached in first opinion practice varies widely. It could be argued that all that is required for a horse to be euthanised due to neoplasia is a strong suspicion on the part of the veterinarian (which would likely be entered in the medical records), irrespective of the final specific diagnosis (if available). Diagnosis (presumptive or definitive) of neoplasia carries grave significance for horse owners, and similar to the other conditions studied here, could influence their behaviour toward early euthanasia. Overlap (co-occurrence) in terminology (cases) between neoplasia, PPID and sarcoids was low to moderate. Between six and seventeen percent of horses categorised under one of these diseases was simultaneously categorised under one of the others (data not shown), lending confidence to the decision to model these conditions separately.

Death in horses rarely occurs naturally, i.e. without euthanasia. An owner's decision to euthanase is very often complex, involving welfare, management, financial and emotional aspects. It can be supposed that diagnosis of a chronic or incurable disease often plays a large part in this decision, but it will rarely be the only reason for euthanasia. In addition, it is common that the precise reason for euthanasia is not noted in medical records (as was the norm in the dataset used here). For these reasons, all-cause mortality was used as the event of interest in these analyses, as cause-specific information was not available. 'Survival times' reported here therefore reflect either survival from diagnosis until natural death (from all causes) or until euthanasia. The use of all-cause mortality is necessary when using data that often omit the cause of death (or include unreliable information), and is also commonly employed in human and animal epidemiologic studies (Black et al., 2002; Tilling et al., 2002; Salles et al., 2004; de Madron et al., 2011; Mattin et al., 2015).

All of the chronic diseases studied were found to significantly affect survival. It is of interest that the hazard ratios for EMS and PPID are so large, and that the expected survival times following diagnosis of these conditions is shorter than most other diseases. Equine metabolic syndrome is a relatively new diagnosis in equine medicine, and, similar to its human counterpart, features metabolic derangements, obesity and insulin resistance (McCue et al., 2015). In horses, the condition has been linked with an increased risk of laminitis. Although EMS is itself not life-threatening, laminitis certainly is through the necessity for euthanasia when welfare is significantly compromised. Similarly, PPID is inextricably linked with laminitis, but does not lead to natural death in the vast majority of cases, therefore it could be supposed that its effect on life expectancy and survival would be modest once laminitis was taken into account. These endocrinopathies have been reported to commonly co-occur, which is a feature of the present dataset (see Table 3) (Donaldson et al., 2004; Karikoski et al., 2011; Ireland et al., 2013). Despite taking breed, age at diagnosis, and co-occurring diseases into account, the effect on mortality of these conditions remains substantial. Far from being 'incidental' features of older age in many horses, these diseases are serious diagnoses that warrant further research.

Co- and multimorbidity were a feature of these data, with 1.2% of horses diagnosed with more than one chronic disease (maximum 6) over the study period. Laminitis was a feature of 74% of all horses with multimorbidity. Laminitis is a painful condition of ungulates where inflammation of the dermal laminae can result in separation of the underlying soft tissue structures from the overlying protective, suspensory hoof wall. The disease is a common sequel to many inflammatory conditions, and exhibits both acute and chronic phases. Given this 'final common pathway' of inflammatory disease, it is perhaps unsurprising that laminitis is so commonly diagnosed alongside other chronic diseases. PPID was a feature in 49% of multimorbid animals, and given this disease's considerable effect on life expectancy and hazard ratios, it constitutes a serious challenge to equine health.

Table 7
Median life expectancy following commencement of lifetime disease co-occurrence status (other independent variables held at their reference or median levels) in a convenience sample of the veterinary-attended UK general horse population.

Lifetime disease co-occurrence status	Median life expectancy in years following commencement of status (95% CI)	Median (IQR) age (years) at commencement of lifetime co-occurrence status
No chronic disease	19.8 (19.4–20.6)	6 (3–12)
One chronic disease	11.5 (10.2–13.5)	14 (7–22)
Two chronic diseases	7.9 (6.6–10.4)	18.5 (11–25)
More than two chronic diseases	1.7 (0.3–9.4)	23 (18–29)

CI confidence interval.

When compared with having none of the chronic diseases studied, co- and multimorbidity were found to pose 6.6 and 21.3 times the hazard of death, respectively (Table 6). This result suggests that co-occurrence of disease within an individual poses additional risk to survival above what may be expected simply by the product of the risk of both diseases individually. Of the conditions studied here, only neoplasia and grass sickness can lead to unassisted death in the horse, thus the deaths of horses suffering from the remaining diseases is likely to be via euthanasia. As mentioned previously, the decision of when to euthanase can be complex, and involves more than simply the levels of pain or distress an animal is experiencing. When a horse is diagnosed with multiple chronic diseases, it is possible that euthanasia is carried out more readily than if that animal only had one disease, due to complexity and difficulty in managing and treating multiple diseases, and/or due to increased costs of treatment. Over the course of this study, the apparent prevalence of multimorbidity was found to increase. Given the significant and increasing apparent prevalence of multimorbidity in this sample, more research into disease clustering and the management of co-occurring diseases is warranted, in order that parsimonious and harmonious treatment regimens can be found for common disease groups, and underlying aetiological commonalities can be better understood (Table 7).

Just as in humans, the average lifespan of veterinary-attended UK horses in this population appears to be increasing overall (Wohland et al., 2015). This result is in agreement with, but offers more validity and robustness to the conclusions of Brosnahan and Paradis (2003), often cited in veterinary literature. The Department of Health of the UK Government often uses comparison of the life expectancy at birth between groups to assess whether a population is ageing. This robust method, employed by the Office for National Statistics, was implemented using the current data. The method allows the user to 'forecast' the life expectancy of horses of different ages, even when the deaths in an age cohort have yet to occur. A significant increase in life expectancy was found between horses born between 2010 and 2012, compared to those born between 1995 and 1997. Given the low overall proportion of horses that died over the entire study (6.7%), it appears that death is often not recorded. For this reason, survival times reported here are useful for comparison between diseases and comorbidity statuses, however their estimated medians should be interpreted cautiously. Brosnahan and Paradis (2003) reported an increase in the proportion of horses of twenty years old or more being presented to a University veterinary clinic between 1989 and 1999 (Brosnahan and Paradis, 2003). The authors concluded that the reason for this increase was unknown, but likely to be multifactorial, and cited greater equine longevity as a likely phenomenon. Increasing willingness on the part of owners to finance veterinary care of geriatric horses was also posited. The referral cases used in the study by Brosnahan and Paradis (2003) are unlikely, however, to be representative of all veterinarian-attended horses, nor of the horse population as a whole. It is possible that the average longevity of horses whose owners had the financial means to access referral care was increasing between 1989 and 1999, but the longevity of horses receiving first-opinion care only, or no veterinary attention, was not. The data used here included a large sample of first-opinion medical records, over a greater timespan, and thus cannot be directly compared to the previous study. Of course, death in this population is very often a result of euthanasia, thus 'survivability' is not the only variable affecting longevity. Financial, management, and welfare aspects all contribute to the decision to end an animal's life.

The results of the current study taken together constitute an important contribution to the understanding of equine epidemiology, and indicate that veterinarians may encounter greater numbers of aged animals in future. Chronic disease is prevalent and of serious concern for equine welfare and longevity, and the apparent prevalence of multimorbidity appears to be increasing. Further study of patterns of multimorbidity in the horse may help to better understand aetiological commonalities and to formulate appropriate management strategies.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.prevetmed.2016.07.011.

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