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1 **Print Summary**

2

3 **QUALITY OF LIFE ASPECTS IN IDIOPATHIC EPILEPSY IN DOGS**

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9

10 **ABSTRACT**

11 Quality of life (QoL) plays a significant role in the treatment of dogs with idiopathic epilepsy  
12 (IE) yet is so far understudied. This study describes the outcome evaluation of an online  
13 questionnaire based on the carer's perception focusing on 62 QoL-questions in 159 dogs with  
14 IE.

15 Results showed that seizure frequency, but not seizure severity or presence of cluster seizures  
16 was significantly associated with carer perceived dog's QoL. Dogs receiving third line  
17 antiepileptic drugs had a significantly lower perceived QoL than those that did not. Generalised  
18 linear mixed model analysis demonstrated that severity of the side effects sleeping more and  
19 ataxia were significantly associated with carer perceived dog's QoL, with higher severities  
20 predicting lower QoL scores. The degree of carer acceptability of seizure frequency and severity  
21 was significantly associated with the dog's reported seizure frequency and severity. Moreover,  
22 there was a significant association between IE-related QoL changes of the dog and the carer,  
23 with reductions in perceived canine QoL scores associated with reductions in carer QoL, and  
24 vice versa.

25 In conclusion, aspects of canine IE can affect both the carer and their dog's QoL. This has  
26 implications for the management and requires consideration when treatment options and  
27 outcomes are discussed.

28

29 **Keywords:** Comorbidity, welfare, seizures, questionnaire

30

31

## 32 INTRODUCTION

33 Canine epilepsy studies mainly focus on the physical aspects of seizures, the impact of  
34 antiepileptic drugs (AED) and more recently also behavioural changes associated with the  
35 disease (Lord and Podell 1999, Chang and others 2006, Shihab and others 2011, Muñana and  
36 others 2012). The physical aspects of canine idiopathic epilepsy (IE) such as seizure frequency  
37 and severity as well as AED side effects are well described, yet the suspected impact on QoL  
38 has only been studied in small numbers of affected dogs. Carers of 37 dogs with IE were mostly  
39 concerned about the dog's QoL, adequate seizure frequency (less than one seizure every three  
40 months) and acceptable side effects of AEDs and that these factors would determine if seizure  
41 control was adequate (Chang and others 2006).

42

43 Neurobehavioral changes are a reported comorbidity of epilepsy in dogs and humans and  
44 include cognitive, behavioural or emotional changes associated with central nervous system  
45 dysfunction. These comorbidities in dogs include increased fear/anxiety, defensive aggression,  
46 abnormal perception, inattention, excitability/impulsivity, and show remarkable similarities to  
47 its human counterpart resembling anxiety and attention deficit hyperactivity disorder (Shihab  
48 and others 2011, Jokinen and others 2015, Packer and others 2016). The carer commonly  
49 assesses non-metric aspects like neurobehavioral changes and QoL aspects based on their  
50 perception (Lord and Podell 1999, Chang and others 2006, Shihab and others 2011, Muñana  
51 and others 2012, Packer and others 2016). The carer's perception of their dog's QoL may be  
52 biased but with this in mind the carer can serve as surrogate. This is an accepted practice not  
53 only in veterinary medicine but also in childhood epilepsy where usually the parent assesses  
54 the QoL of the epileptic child (Liu and Han 2015). It is further known that not only the QoL of  
55 the affected child but also of their carer can be affected in childhood epilepsy. Parents of  
56 epileptic children showed significantly lower QoL scores, and higher levels of depression and

57 anxiety correlating to seizure control, employment, financial implications of caring for an  
58 individual with epilepsy, the occurrence of status epilepticus, drug side effects and age of  
59 parents among others (Lv and others 2009). Information about the impact of caring for an  
60 epileptic dog on the carer's QoL is limited yet effect on the carer's day-to-day activities and  
61 their free time are describes (Lord and Podell 1999, Chang and others 2006).

62

63 Wessmann et al. (2014) published the creation of a disease-specific QoL questionnaire in dogs  
64 with IE and their carers (EpiQoL). The questionnaire design was based on the multidimensional  
65 aspects of QoL as defined by the WHO into physical, social, and neurobehavioral (dog) /  
66 psychological health aspects (carer) adapted for IE (Wessmann and others 2014). The current  
67 study explores the actual data and factors that affect QoL in dogs with IE and their carers with  
68 seven hypotheses (H1-H7) utilising data from Wessmann and others (2014). The QoL measures  
69 in this study largely focused on the carer's perception of their dog's and their own QoL.

70

71 H1: The seizure phenotype (frequency of seizure days, severity) affects the carer's perception  
72 of QoL in canine IE patients.

73 H2: There is an effect of being treated with certain AEDs upon carer perception of canine  
74 epilepsy.

75 H3: Side effects of AEDs impact upon carer perception of canine QoL.

76 H4: The reported severities of AED side effects are associated with the degree of carer  
77 acceptability of AED side effects.

78 H5: A dog's seizure frequency is associated with the degree of carer acceptability of seizure  
79 frequency.

80 H6: A dog's seizure severity is associated with the degree of carer acceptability of seizure  
81 severity.

82 H7: There is an association between changes in carer QoL and carer perception of their dog's  
83 QoL following the onset of IE.

84

## 85 **MATERIAL AND METHODS**

86 Carers of dogs diagnosed with IE were recruited at the authors' institutions (UGVS, RVC) by  
87 paper mail stating a link to the online questionnaire, through contacting 800 primary care  
88 practices by email and through a canine epilepsy website ([www.canineepilepsy.co.uk](http://www.canineepilepsy.co.uk)). Data was  
89 acquired from January to November 2011. Dogs were included if they presented with recurrent  
90 seizures (two or more) at least one month apart which were either presumptively diagnosed  
91 with IE following substantial investigation, including normal brain imaging (MRI or CT) and  
92 cerebrospinal fluid analysis independent of the age of onset or strongly suspected to have IE  
93 with seizures for more than one year and an age of onset between 6 months to 6 years.  
94 Responses were excluded if other diseases that required ongoing veterinary treatment or  
95 attention were reported or if the dog was not alive at the time of completion of the questionnaire  
96 (Wessmann and others 2014).

97 This study reports the outcome of 36 key questions (EpiQoL) associated with IE in 159 affected  
98 dogs and their carer's, as previously described by the authors (Supplementary file A, Wessmann  
99 and others 2014). Items such as seizure severity, frequency and side effects of AEDs were  
100 considered to affect the physical aspects of the dog. The seizure frequency considered the  
101 'seizure days' on which seizures occurred and therefore could include single and multiple  
102 seizures ('cluster') for this day. Items such as restrictions and frustrations on the carer's life  
103 such as limitations in work, education, day-to-day activities, and social life because of caring  
104 for an epileptic dog were grouped under the social aspects affecting the carer. Psychological  
105 health aspects affecting the carer included items such as the carer's distaste of AED side effects  
106 and carer anxiety around the seizure frequency and severity and its effects on the dog

107 (Supplementary file A). Twenty-six additional questionnaire items from the original project  
108 questionnaire were included such as direct QoL focused questions, descriptive data around the  
109 seizure event, psychological health aspects of the carer concerning mainly the dog's health and  
110 the effect on the carer (Supplementary file B). A total of 62 questions were used to test the  
111 aforementioned hypotheses.

112

### 113 *Statistical analysis*

114 To investigate the above seven questions, three carer-reported proxies of canine QoL were used  
115 as outcome measures:

116 (i) A score from 1-10 (treated as continuous, with 1 being the worst and 10 being the best);

117 (ii) QoL in the past three months (categorical from pretty bad-very well); and

118 (iii) Change in QoL since the onset of epilepsy (categorical from much decreased-much  
119 increased).

120 Independent dog-related variables included aspects of the seizure phenotype: seizure frequency  
121 (seizure days), seizure severity and the occurrence of cluster seizures; AED treatment and the  
122 severity of side effects encountered. Carer-related independent variables included the degree of  
123 carer acceptability (rated from strong agreement – strong disagreement) of seizure frequency  
124 and severity, and carer reported QoL change since the onset of epilepsy (categorical from much  
125 decreased-much increased). Kruskal-Wallis and Mann-Whitney U tests were used to test for  
126 associations between outcome measure (i) and independent variables, and Chi-squared analysis  
127 for associations between outcome measures (ii) and (iii) and independent variables. Where  
128 indicated by univariate analyses ( $p < 0.10$ ), generalised linear mixed model (glmm) analyses  
129 were carried out, with breed taken into account as a random effect. Multicollinearity was  
130 checked for in all models, identified from inflated standard errors in the models, and thus

131 avoided. Model fit was assessed using the deviance and Akaike's information criterion. All tests  
132 were used two-sided with  $P < 0.050$  being considered statistically significant.

133

## 134 **RESULTS**

135 One hundred-and-fifty-nine dogs of 50 breeds met the inclusion criteria. Mean age was 5.8  
136 years (median 5.2 years, range 0.7-12.5 years), with 66 female (52 neutered) and 93 male dogs  
137 (67 neutered). The mean age of onset of seizures was 2.7 years (median 2 years, range 0.3-9.0  
138 years).

139

140 The results of the 36 key questions and the additional 26 questionnaire items are displayed in  
141 Supplementary file A and B respectively. The answers to the seven carer perceived QoL  
142 questions are as follows:

143

144 *H1: The seizure phenotype (frequency of seizure days, severity) affects the carer's perception*  
145 *of QoL in canine IE patients.*

146 Of the three measures of seizure phenotype (seizure frequency, severity and presence of cluster  
147 seizures), only one measure, seizure frequency, was significantly associated with carer  
148 perceived dog's QoL, when scored out of ten (Kruskal-Wallis=17.5,  $p=0.014$ ), when rated for  
149 the past three months categorically ( $X^2=38.8$ ,  $p=0.003$ ), and when questioned about how it has  
150 changed since the onset of IE ( $X^2=41.2$ ,  $p=0.016$ ). Higher seizure frequencies were associated  
151 with decreased carer perceived dog's QoL measures, with the median QoL score for dogs  
152 experiencing less than one seizure day every six months scoring 9 (range 5-10), 41.4% of carers  
153 perceived their dog's QoL as 'very well: could hardly be better' and 51.7% stating their dog's  
154 QoL had stayed the same since the onset of epilepsy. In contrast, dogs experiencing 'more than  
155 one seizure day every week' had a median QoL score of 7.5 (range 4-8), with no carers reporting



156 their dog's QoL 'very well: could hardly be better' and the majority (87.5%) stating their dog's  
157 QoL had 'decreased a little' since the onset of epilepsy. There were no associations between  
158 seizure severity and the presence of cluster seizures with any measure of QoL ( $p>0.050$ ).

159

160 *H2: There is an effect of being treated with certain AEDs upon carer perception of canine*  
161 *epilepsy.*

162 There was no difference in carer perceived dog's QoL scored out of ten or in the past three  
163 months between dogs receiving phenobarbital or not, potassium bromide or not, or diazepam  
164 or not ( $p>0.050$ ). When QoL was considered since the onset of epilepsy, dogs that received  
165 phenobarbital were rated by their carers to have had a reduction in QoL compared to those that  
166 did not (55.6% vs. 25.7% rated their dog's QoL to be 'a little decreased' since the onset of  
167 epilepsy, respectively;  $p=0.008$ ), as were dogs that received potassium bromide in comparison  
168 to those that did not (60.5% 'a little decreased' vs. 36.8%, respectively;  $p=0.017$ ). When the  
169 number of AEDs administered was considered, there was a significant difference in carer  
170 perceived dog's QoL between dogs being treated with third line drugs or not, when scored out  
171 of ten (Mann-Whitney= 1545,  $p=0.002$ ), rated for the past 3 months categorically ( $X^2= 10.8$   
172  $p=0.013$ ), and when questioned about how it has changed since the onset of IE ( $X^2= 13.5$ ,  
173  $p=0.009$ ), with dogs receiving third line drugs having a reduced QoL compared to those that do  
174 not.

175

176 *H3: Side effects of AEDs impact upon carer perception of canine QoL (Table 1)*

177 The severity of four of the eleven reported AED side effects were significantly associated with  
178 carer perceived dog's QoL at the univariate level: 'drinking more' (Kruskal-Wallis (KW): 15.5,  
179  $p=0.008$ ), 'sleeping more' (KW: 14.8,  $p=0.011$ ), 'wobbly/not coordinated when walking' (KW:  
180 16.3,  $p=0.006$ ) and 'restlessness/pacing' (KW: 21.0,  $p=0.001$ ). Dogs that were not affected by

181 'drinking more' had a median carer perceived QoL score of 9.0 (range 7.0-10.0), whereas those  
182 reported to be very severely affected had a median of 8.0 (range 3.0-10.0). Dogs that were not  
183 affected by 'sleeping more' had a median carer perceived QoL score of 9.0 (range 5.0-10.0),  
184 whereas those reported to be very severely affected had a median of 8.0 (range 4.0-10.0). Dogs  
185 that were not affected by 'wobbliness/not coordinated when walking' had a median carer  
186 perceived QoL score of 9.0 (range 6.0-10.0), whereas those reported to be very severely affected  
187 had a median of 8.0 (range 5.0-10.0). Finally, dogs that were not affected by  
188 'restlessness/pacing' had a median carer perceived QoL score of 9.0 (range 3.0-10.0), whereas  
189 those reported to be very severely affected had a median of 8.0 (range 3.0-10.0). These four  
190 factors were tested in a generalised linear mixed model (glmm) with breed taken into account  
191 as a random effect. While four factors were significantly associated with QoL at the univariate  
192 level as stated above, only two factors remained significant when included together in a glmm  
193 showing the largest effect on QoL that was not explained by the other variables. These two  
194 factors significantly predicted carer perceived dog's QoL: the severity of 'sleeping more' and  
195 the severity of being 'wobbly/not coordinated when walking' ( $p < 0.050$ ). The less severely the  
196 dog was affected by 'sleeping more' or being 'wobbly/not coordinated', the higher (better) the  
197 carer perceived dog's QoL score.

198

199 *H4: The reported severities of AED side effects are associated with the degree of carer*  
200 *acceptability of AED side effects.*

201 The severity of seven of the eleven reported AED side effects (rated from 1-5: very mild – very  
202 severe) were significantly associated with carer reported acceptability of side effects (rated from  
203 1-5: strongly agree – strongly disagree) at the univariate level: 'eating more', 'gaining weight',  
204 'drinking more', 'urinating more', 'sleeping more', 'wobbly/not coordinated when walking'  
205 and 'restlessness/pacing' ( $p < 0.050$ ). Increased severity of these side effects was associated with

206 a decreased level of carer acceptability. There was no association between the severity of  
207 'itchiness/skin rash', 'vomiting', 'diarrhoea' and 'coughing' and carer-rated acceptability of  
208 side effects ( $p>0.050$ ).

209

210 *H5: A dog's seizure frequency is associated with the degree of carer acceptability of seizure*  
211 *frequency.*

212 Seizure frequency was significantly associated with the degree of carer acceptability of seizure  
213 frequency ( $X^2=100.5$ ,  $p<0.001$ ), with carers reporting higher seizure frequencies disagreeing  
214 more that their dogs seizure frequency was acceptable and vice versa. For example, 46.4% of  
215 the carers of dogs experiencing 'less than one seizure day every six months' strongly agreed  
216 their dog's seizure frequency was acceptable, whereas no carers of dogs experiencing 'more  
217 than one seizure day every week' strongly agreed their dog's seizure frequency was acceptable,  
218 with 75.0% strongly disagreeing.

219

220 *H6: A dog's seizure severity is associated with the degree of carer acceptability of seizure*  
221 *severity.*

222 Seizure severity was significantly associated with the degree of carer acceptability of seizure  
223 severity ( $X^2=100.9$ ,  $p<0.001$ ), with carers reporting higher seizure severities disagreeing more  
224 that their dog's seizure severity was acceptable and vice versa. For example, 37.5% of the carers  
225 of dogs experiencing 'mild' seizures strongly agreed their dog's seizure severity was  
226 acceptable, whereas only 4.8% of carers of dogs experiencing 'very severe' seizures strongly  
227 agreed, with 61.9% strongly disagreeing that this severity was acceptable.

228

229 *H7: There is an association between changes in carer QoL and carer perception of their dog's*  
230 *QoL following the onset of IE.*

231 There was a significant association between the change in carer perceived dog's QoL after the  
232 onset of IE and the change in the carer's QoL after the onset of IE ( $X^2=101.7$ ,  $p<0.001$ ), with  
233 carers reporting their dog's QoL had decreased more likely to report that their QoL had  
234 decreased too, and vice versa. No carers of dogs whose perceived QoL had 'much decreased'  
235 after the onset of epilepsy reported their own QoL was 'increased' or 'much increased' (0.0%),  
236 with 50.0% stating their QoL was also 'much decreased'. Participants commented on suffering  
237 to some degree from depression or panic attacks (29.0%) and feeling isolated (22.0%) as a result  
238 of caring for an epileptic dog (Supplementary file B). In contrast, the majority (71.4%) of carers  
239 who perceived their dog's QoL was 'much increased' after the onset of epilepsy reported their  
240 own QoL was also 'much increased'.

241

## 242 **DISCUSSION**

243 Of the three measures of seizure phenotype (seizure frequency, severity and presence of cluster  
244 seizures), only one measure, seizure frequency (seizure days), was significantly associated with  
245 QoL as perceived by the dog's carer in this study. Chang and others (2006) reported that carers  
246 of 29 dogs referred to one institution perceived a seizure frequency of 'one seizure every three  
247 to six months' to be most reasonable for their pet. Most participants in the current study  
248 perceived only a 'seizure-free' state acceptable for their pet (Supplementary file B). Similarly,  
249 freedom from seizures is the treatment goal in people (Lee 2014). It was shown that seizure  
250 frequency is one of the main risk factor for decreased QoL in children with epilepsy (Liu and  
251 Han 2015). A significant correlation between seizure severity and the carer's perception of their  
252 dog's QoL could not be established. The statistical analysis did not show whether a history of  
253 'cluster seizures' was associated with the dog's QoL. It appears that the frequency but not their  
254 temporal density was important to carer perceived QoL of their dog. It would appear reasonable  
255 to assume that cluster seizures and status epilepticus impact on the perceived dog's QoL, given

256 that the occurrence of cluster seizures and status epilepticus increased the risk of epilepsy  
257 related euthanasia in previous studies (Saito and others 2001, Monteiro and others 2012, Fredso  
258 and others 2014). This might be related to the fact that the QoL scores are a reflection of the  
259 carer's perception of their dog's QoL as a proxy of the dog's actual QoL.

260

261 The use of two common types of AED (phenobarbital and potassium bromide) had a negative  
262 effect on carer's perception of their dog's QoL when considered since the onset of epilepsy,  
263 and there was an effect of the number of AEDs administered, with dogs being treated with third  
264 line drugs experiencing a reduced carer perceived QoL compared to those with 1-2 AEDs. Both,  
265 seizure control and number of medications administered, are significantly associated with QoL  
266 in epileptic children (Williams and others 2003). Drug-resistance is frustrating and challenging  
267 to manage. The probability of seizure control is reduced with successive AED treatment (Lee  
268 2014, Packer and others 2015). Response rates in people with epilepsy for the first, second or  
269 third-line AED as proportion of the population were 47-50%, 10-13% and 2-4% respectively  
270 (Kwan and Brodie 2000, Mohanraj and Brodie 2006). Similarly, in dogs with epilepsy, the  
271 response rate as proportion of the population for first, second and third line AEDs was 37%,  
272 11% and 6% respectively (Packer and others 2015). There was an association between both  
273 seizure frequency and severity and carer-perceived acceptability of these traits, with higher  
274 seizure frequencies and severities perceived to be less acceptable by carers. Drug-resistance  
275 remains a main cause of epilepsy related euthanasia in canine IE (Chang and others 2006,  
276 Fredso and others 2014, Wessmann and others 2014). Although freedom from seizures is one  
277 of the main goals of epilepsy therapy in people (Lee 2014), it is not easily achieved, and with  
278 as few as 14% of treated dogs achieving remission in hospital dog populations (Packer and  
279 others 2014) the management of carer's expectations by their veterinarians is vital for  
280 understanding the outcomes of therapy.

281  
282 The AED side effects that impact on the dog's QoL and their acceptability by the carer vary  
283 between the 11 investigated side effects. Only the AED side effects 'sleeping more' and the  
284 severity of being 'wobbly/not coordinated when walking' significantly predicted carer  
285 perception of their dog's QoL in a multivariate analysis. 'Drinking more' and  
286 'restlessness/pacing' had further a significant influence on the dog's QoL at a univariate level.  
287 However, increased severity of these side effects 'eating more', 'gaining weight', 'drinking  
288 more', 'urinating more', 'sleeping more', 'wobbly/not coordinated when walking' and  
289 'restlessness/pacing' were associated with a decreased level of carer acceptability. The variety  
290 of the different side effects may explain discrepancies to previous studies. One study reported  
291 that phenobarbital therapy appeared to have minimal side effects on the overall carer perceived  
292 QoL of the studied dog population and thus did not produce a significant problem for the carers  
293 (Lord and Podell 1999), whereas another study reported that acceptable side effects were one  
294 of the greatest concerns for carers (Chang and others 2006). The presence of side effects is an  
295 outcome measure for successful AED therapy in people (Lee 2014). Newer AEDs commonly  
296 fail to show better efficacy than older AEDs. Thus, the selection of the first-line drug is mostly  
297 lead by the characteristics and frequency of the AED side effects (Lee 2014). With the advent  
298 of newer AEDs in veterinary medicine AED side effects have the potential to drive drug  
299 selection, given the perceived impact of the side effects on the QoL of the dog by the carer.  
300 Despite multiple AEDs being available in human medicine, there remains a need for new AEDs  
301 in canine and human epilepsy with fewer side effects, increased efficacy, drugs with different  
302 mechanism of action with the potential of synergistic combination therapy (Lee 2014). On the  
303 other hand, third AED currently used in veterinary medicine have largely not been through  
304 clinical trials in dogs to test their efficacy. Therefore one could question the necessity of finding  
305 even newer if the available ones have not been tested.

306

307 The change in the carer's perception of their dog's QoL was significantly associated with the  
308 change in the carer's QoL after the onset of IE. Carers reporting a decreased QoL in their dogs  
309 were more likely to report that their QoL had also decreased. This response reflects a well-  
310 known phenomenon in childhood epilepsy, where the disease not only affects the QoL of the  
311 affected child but also of the carer, usually their parent (Cushner-Weinstein and others 2008,  
312 Lv and others 2009). The factors correlated with parental QoL were seizure control, status  
313 epilepticus, drug side effects, the degree of the child's anxiety and depression (Lv and others  
314 2009). Lack of control over events, unpredictability of events, sleep deprivation and a feeling  
315 of helplessness are known factors in the development of stress in people (Henn and Vollmayr  
316 2005, Koolhaas and others 2011) and epilepsy influences some, if not all of these factors.  
317 Moreover, up to 50% of mothers are at risk of clinical depression as a consequence caring for  
318 an epileptic child (Ferro and Speechley 2009). Similarly, canine IE can also impact on the  
319 mental health of the carer. A small number of participants commented on suffering to some  
320 degree from depression or panic attacks and feeling isolated as a result of caring for an epileptic  
321 dog (Supplementary file B). Noteworthy is that an improved carer perceived dog's QoL resulted  
322 also in an improved QoL of the carer demonstrating potentially positive aspects of IE treatment.  
323 This positive finding associated with IE is encouraging and may reflect an enhanced connection  
324 between diseased pet and carer observed for cats with diabetes mellitus and their carers (Niessen  
325 and others 2010).

326

327 This study showed on a large scale, that canine IE has not only an effect on the perceived QoL  
328 of the affected dog but is also significantly associated with the carer's perceived QoL. Carers  
329 reporting a decreased QoL in their dogs were more likely to report that their QoL had decreased  
330 too. Seizure frequency, severity of AED side effects sleeping more and ataxia and dogs

331 receiving third line AEDs were associated with the carer perceived dog's QoL, with higher  
332 severities predicting lower QoL scores. Thus, optimising seizure control and AED therapy will  
333 not only affect the perceived QoL of the affected dog but also of the carer. The carer's QoL  
334 affected by caring for an epileptic dog is an important part of IE treatment as the perceived  
335 impact of IE not only on the dogs' but also on the carers' QoL is likely to influence a carer's  
336 choices regarding treatment or euthanasia and requires consideration when treatment options  
337 are discussed.

338

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342

343



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435 **LEGENDS**

436

437 **Table 1. Impact of antiepileptic drug side effects upon carer perceived dog's quality of life**

438 **score.** The factors 'drinking more', 'sleeping more', 'wobbly/not coordinated when walking'  
439 and 'restlessness/pacing' were tested in a generalised linear mixed model (glmm) with breed  
440 taken into account as a random effect. The severity of 'sleeping more' and the severity of being  
441 'wobbly/not coordinated when walking' ( $p < 0.050$ ) significantly predicted carer perceived  
442 dog's QoL. The less severely the dog is affected by 'sleeping more' or being 'wobbly/not  
443 coordinated when walking', the higher the carer perceived dog's QoL score.

444

445 **Supplementary file A.** Outcome of 7 themes with 36 key questions from a disease-specific IE  
446 online questionnaire as previously published by Wessmann and others (2014).

447

448 **Supplementary file B.** Outcome of 26 complementary questionnaire items as previously  
449 published by Wessmann and others (2014).

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453 **Table 1. Impact of antiepileptic drug side effects upon carer perceived dog's quality of life**  
454 **score.** The factors 'drinking more', 'sleeping more', 'wobbly/not coordinated when walking'  
455 and 'restlessness/pacing' were tested in a generalised linear mixed model (glmm) with breed  
456 taken into account as a random effect. The severity of 'sleeping more' and the severity of being  
457 'wobbly/not coordinated when walking' ( $p < 0.050$ ) significantly predicted carer perceived  
458 dog's QoL. The less severely the dog is affected by 'sleeping more' or being 'wobbly/not  
459 coordinated when walking', the higher the carer perceived dog's QoL score.  
460

<b>Risk factor</b>	<b>Sub-category</b>	<b>Coefficient (95% CI)</b>	<b>SE</b>	<b>t</b>	<b>P value</b>
Intercept	-	5.7 (4.5-6.9)	0.6	9.2	0.000
Sleeping more	Side effect not present	1.7 (0.4-2.9)	0.6	2.6	0.010
	Very mild	1.3 (-0.1-2.6)	0.7	1.8	0.072
	Mild	1.5 (0.2=2.9)	0.7	2.2	0.030
	Moderate	1.0 (-0.3-2.3)	0.6	1.96	0.114
	Severe	1.4 (-0.1-2.8)	0.8	1.8	0.702
	Very severe	<i>Reference</i>			
Wobbly/not coordinated when walking	Side effect not present	1.4 (0.4-2.4)	0.5	2.8	0.006
	Very mild	1.1 (-0.0-2.1)	0.5	2.0	0.053
	Mild	0.7 (-0.5-1.8)	0.6	1.1	0.258
	Moderate	0.3 (-0.8-1.4)	0.6	0.6	0.553
	Severe	0.9 (-0.3-2.1)	0.6	1.5	0.138
	Very severe	<i>Reference</i>			

461 CI, confidence interval; SE, standard error

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