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1	Prevalence and breed predisposition for thoracolumbar intervertebral disc disease in cats
2	Steven De Decker, Anne-Sophie Warner, Holger A Volk.
3	Clinical Science and Services, The Royal Veterinary College, University of London, Hatfield,
4	UK
5	
6	Corresponding author: Steven De Decker, DVM, PhD, DipECVN, MvetMed, FHEA, MRCVS
7	Email: <u>sdedecker@rvc.ac.uk</u>
8	Address: Clinical Science and Services, The Royal Veterinary College, University of London,
9	Hawkshead Lane, North Mymms, Hatfield, Hertfordshire, AL9 7TA, UK
10	Tel: +44(0)1707 666366
11	Fax: +44 (0)1707 649384
12	
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20	
21	

#### 22 Abstract

*Objectives*: to evaluate the prevalence and possible breed predilections for thoracolumbar
 intervertebral disc disease (IVDD) in cats.

*Methods*: Medical records and imaging studies of cats diagnosed with thoracolumbar IVDD were retrospectively reviewed and compared to the general hospital population between January 2008 and August 2014. The association between type of IVDD [i.e. intervertebral disc extrusion (IVDE) or intervertebral disc protrusion (IVDP)] and breed, age, gender, duration and severity of clinical signs was also evaluated.

30 *Results*: Of 12900 cats presented during the study period, 31 (0.24%) were diagnosed with 31 IVDD, including 17 purebred and 14 non-purebred cats. Of all presented purebred cats, 0.52% were diagnosed with thoracolumbar IVDD. More specifically, 1.29% of all British Shorthairs 32 and 1.83% of all presented Persians were diagnosed with IVDD. Compared to the general 33 hospital population, purebred cats (P=0.0001), British Shorthairs (P<0.0001) and Persians 34 35 (P=0.0006) were significantly overrepresented with thoracolumbar IVDD. Affected purebred cats were younger compared to affected non-purebred cats (P=0.02). Of 31 cats with IVDD, 36 37 19 were diagnosed with IVDE and 12 with IVDP. Cats with IVDE had a significantly shorter 38 duration of clinical signs (P=0.0002) and demonstrated more severe neurological deficits 39 (P=0.04) compared to cats with IVDP.

40 *Conclusions and relevance*: Although thoracolumbar IVDD is an uncommon condition in cats,
41 purebred cats, British Shorthairs, and Persians were overrepresented. It is currently unclear if
42 this represents a true breed predisposition or a higher likelihood of owners of purebred cats to
43 seek referral for advanced diagnostic imaging procedures.

44

#### 46 Introduction

Although our knowledge of feline spinal cord diseases has increased continuously over years, 47 the diagnosis and treatment of the most common spinal disease processes, such as feline 48 49 infectious peritonitis and lymphoma, remain challenging<sup>1,2</sup>, while less common feline spinal 50 disorders still need to be better characterised. A previous study, evaluating the prevalence of histologically confirmed spinal disorders in cats, demonstrated that inflammatory/infectious 51 52 diseases represent the most common feline spinal disorders, followed by neoplastic and 53 traumatic disease processes. Intervertebral disc disease (IVDD) represented only 4% of all cats with a spinal cord disorder<sup>3</sup>, while another study indicated that of 92 cats undergoing spinal 54 MRI, only 5 were diagnosed with IVDD.<sup>1</sup> It is therefore not surprising that only a limited 55 number of studies have described the clinical characteristics of feline degenerative IVDD.<sup>4-10</sup> 56 57 Its prevalence is considered low, no breed or sex predilection has been reported, affected cats are generally older, and prognosis after surgical decompression is considered good.<sup>2,8,9</sup> 58 Although both intervertebral disc extrusions (IVDE), or Hansen type-I IVDD, and 59 intervertebral disc protrusions (IVDP), or Hansen type-II IVDD, have been reported <sup>5,9</sup>, its 60 currently unclear if both types of IVDD are associated with different disease characteristics in 61 62 cats. The situation is different in dogs. Degenerative IVDD is considered the most common and best-characterised canine spinal condition.<sup>11</sup> Numerous studies have evaluated the 63 prevalence of thoracolumbar IVDD among the overall canine population <sup>12</sup>, breed-specific risk 64 factors have been identified <sup>12,13</sup>, and several studies have reported disease characteristics for 65 dogs with thoracolumbar IVDE or IVDP.<sup>14,15</sup> The overall goal of this study was therefore to 66 evaluate the clinical presentation of feline thoracolumbar IVDD. More specifically the aims of 67 68 this study were to assess the prevalence and potential breed predisposition of feline thoracolumbar IVDD and evaluate if IVDE and IVDP would be associated with different 69 70 disease characteristics. It was hypothesised that the prevalence of feline thoracolumbar IVDD

would indeed be low, that purebred cats would have an increased risk to suffer from IVDD,
and, similar to the situation in dogs, thoracolumbar IVDE and IVDP would be associated with
different disease characteristics.

74

#### 75 Material and Methods

76 The digital medical database of the small animal referral hospital, Royal Veterinary College, 77 University of London was searched for cats diagnosed with thoracolumbar IVDD between January 2008 and August 2014. Search terms included 'intervertebral disc disease', 'disc 78 79 extrusion', 'disc protrusion', 'disc herniation' and 'disc prolapse'. Thoracolumbar IVDD was 80 defined as IVDE or IVDP between the first thoracic (T1) and seventh lumbar (L7) vertebra. 81 Cats were included if the clinical presentation and magnetic resonance imaging (MRI) studies were both suggestive for degenerative IVDD and if the medical records and imaging studies 82 were available for review. Cats were excluded if the medical records or imaging studies were 83 84 incomplete or not available for review. Before inclusion, a board-certified neurologist (SDD) reviewed all medical records and imaging studies to evaluate diagnostic accuracy. The 85 86 following information was retrieved from the medical records: clinical history, signalment, 87 duration, type, and severity of clinical signs, general physical and neurological examination findings, and type of treatment initiated after diagnosis. Type of clinical signs was recorded as 88 spinal hyperaesthesia, ambulatory paraparesis, non-ambulatory paraparesis, or paraplegia as 89 the predominant clinical sign. Gradation of severity of neurological deficits was based on the 90 modified Frankel score <sup>16</sup>, and was defined as paraplegia without nociception (grade 0), 91 92 paraplegia with nociception (grade 1), non-ambulatory paraparesis (grade 2), ambulatory 93 paraparesis and ataxia (grade 3), spinal hyperaesthesia only (grade 4), or no dysfunction. For 94 all included cats, a 1.5T MRI unit (Intera, Philips Medical Systems) was used to obtain a

95 diagnosis of IVDD. Magnetic resonance imaging was performed under general anaesthesia and 96 included a minimum of T2-weighted (repetition time [RT] [ms], echo time [TE], [ms] 97 3333/110) and T1-weighted (TR/TE, 515/15) sagittal and transverse images. Selected products 98 for induction and maintenance of general anaesthesia were at the discretion of the anaesthetist 99 responsible for the case. The location and number of affected intervertebral disc spaces were 100 noted and each intervertebral disc herniation was further characterised as IVDE (or Hansen Type-I disc disease) or IVDP (or Hansen Type-II disc disease). The differentiation between 101 IVDE and IVDP was based on previously evaluated MRI criteria<sup>15</sup> and where possible; the 102 103 type of IVDD was verified by the surgical reports. More specifically, MRI findings compatible 104 with midline instead of lateralised intervertebral disc herniation and partial instead of complete 105 intervertebral disc degeneration were considered suggestive for IVDP, while a single instead 106 of multiple intervertebral disc herniation and dispersed disc material not confined to the 107 boundaries of the affected intervertebral disc space were considered suggestive for IVDE.<sup>15</sup> 108 Although evaluation of treatment was beyond the scope of this study, medical management 109 typically consisted of a combination of strict rest for 4 weeks and non-steroidal anti-110 inflammatory drugs, followed by gradual increase in activity over the following 4-6 weeks. Surgical management consisted of a decompressive hemilaminectomy. 111

112 Data analysis was performed using standard statistical software package (Prism 6, GraphPad 113 Software Inc., La Jolla, CA). A chi-square test was used to compare the prevalence of purebred 114 and non-purebred cats and to evaluate the prevalence of breeds that were included more than 115 twice in the list of affected breeds (Domestic shorthair, Domestic longhair, British shorthair, and Persian). A Mann Whitney U test was used to compare age, weight, duration of clinical 116 117 signs, and grade of neurological deficits between cats with IVDE and IVDP. A Fisher's exact test was used to compare gender and presence of spinal hyperaesthesia between cats with IVDE 118 119 and IVDP. Values of P < 0.05 were considered statistically significant.

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#### 121 Results

Of 12900 cats presented during the study period at our referral hospital, 31 were diagnosed 122 123 with IVDD, including 17 purebred and 14 non-purebred cats. Included breeds were Domestic 124 shorthair, Domestic longhair, British shorthair, Persian, Bengal, Siamese, Havana Brown, 125 Maine Coon, Sphynx, and American Shorthair (Table 1). The prevalence of IVDD during the 126 study period was 0.24% for all presented cats overall, 0.15% for all presented non-purebred 127 cats, 0.52% for purebred cats, 1.83% for Persians, and 1.29% for British shorthairs. Compared 128 to the overall feline population, purebred cats (P=0.0001), British shorthairs (P<0.0001), and 129 Persians (P=0.0006) were significantly overrepresented. The group of affected cats included 130 16 neutered males and 15 neutered females aged between 9 months and 12 years and 4 months 131 (mean, 9 years and 6 months; median, 9 years). The cat affected at 9 months of age had 132 surgically confirmed IVDE. Affected purebred cats were significantly younger than affected non-purebred cats. Included purebred cats were aged between 9 months and 13.7 years 133 134 (median, 7.6 years), while affected non-purebred cats were aged between 1.3 and 15.3 years 135 (median, 12.2 years). Duration of clinical signs ranged from 12 hours to 6 years (mean, 120 days; median, 15 days) and included spinal hyperaesthesia (n=4), ambulatory paraparesis 136 137 (n=17), non-ambulatory paraparesis (n=6), and paraplegia (n=4) as the predominant clinical 138 sign. In 23 of 31 cats spinal hyperaesthesia could be elicited on spinal palpation. Severity of 139 neurological deficits varied from grade 0 (n=2), grade 1 (n=2), grade 2 (n=6), grade 3 (n=17), 140 and grade 4 (n=4). There were no significant differences between purebred and non-purebred 141 cats for bodyweight gender, duration and type of clinical signs, severity of neurological deficits, or presence of spinal hyperaesthesia (P>0.05). Magnetic resonance imaging 142 143 demonstrated a total of 33 intervertebral disc herniations in 31 cats; a single intervertebral disc herniation was seen in 29 cats and two separate intervertebral disc herniations in 2 cats. The 144

145 most affected intervertebral disc space was L2-L3 (n=6), followed by T11-T12 (n=5), L3-L4, 146 L6-L7 (n=4 for each), T12-T13, T13-L1, L1-L2 (n=3 for each), T2-T3 (n=2), T8-T9, T9-T10, 147 and L5-L6 (n=1 for each). Of 31 cats with IVDD, 19 were diagnosed with IVDE and 12 with 148 IVDP. Cats with IVDE had a significantly longer duration of clinical signs (mean duration of 149 clinical signs 4 versus 72 days; P=0.0002) and demonstrated more severe neurological deficits 150 (mean neurological grade of 3.2 versus 4.1; P=0.04) compared to cats with IVDP. There was no significant influence of breed, gender, age, or the presence of spinal hyperaesthesia on the 151 type of intervertebral disc herniation (P>0.05). Fifteen cats underwent surgery, 14 cats 152 153 underwent medical management, and 2 cats were euthanised at the moment of diagnosis without treatment attempted. Surgery confirmed the suspected type of intervertebral disc 154 155 herniation (IVDE or IVDP) on each occasion. The surgical appearance of IVDE was 156 characterised as sequestered calcified intervertebral disc material without physical connection with the ruptured anulus fibrosus. The surgical appearance of IVDP was characterised by a 157 158 focal or broad based dorsal displacement of the intervertebral disc without any defect in the 159 outer layers of the anulus fibrosus.

160

#### 161 **Discussion**

This study evaluated the prevalence, possible breed predisposition, and clinical presentation of thoracolumbar IVDD among a population of cats referred to a university teaching hospital. Our results confirm that degenerative IVDD should be considered a rare condition in cats. The prevalence of this disorder was only slightly higher than reported previously.<sup>9</sup> It was 0.24% in the current study, while a previous study documented a prevalence of 0.12% of all cats presented at a North American university teaching hospital.<sup>9</sup> Although other reasons cannot be excluded, this possibly reflects continuous developments in veterinary medicine with advanced 169 imaging procedures, including MRI, performed in an increasing number of cats. Alternatively, 170 the results of our study suggest a possible breed predisposition for feline thoracolumbar IVDD. 171 It can therefore not be excluded that differences in breed distribution among geographical 172 locations has contributed to a difference in disease prevalence. It is currently unclear why cats are only rarely affected by IVDD compared to other domesticated small animals, such as 173 dogs.<sup>12</sup> A recent study, evaluating the histopathological characteristics of the feline 174 intervertebral disc identified possible feline-specific changes in the anulus fibrosus.<sup>17</sup> While 175 the nucleus pulposus demonstrated histological changes comparable to those found in canine 176 177 intervertebral discs, the feline anulus fibrosus showed distinct depositions of 178 glycosaminoglycans and contained a high degree of chondrocyte-like cells ranging into the outer anulus fibrosus.<sup>17</sup> It is currently however unclear if these changes indeed protect the feline 179 180 intervertebral disc against degeneration and herniation.

181 In agreement with previous studies, the domestic shorthair was the most common breed to have thoracolumbar IVDD.<sup>2,8,9</sup> However, when taking the relative popularity of the presented breeds 182 into account, purebred cats were significantly overrepresented. More specifically, Persians and 183 British shorthairs were more commonly diagnosed with thoracolumbar IVDD compared to 184 185 other breeds. It is currently unclear why these specific purebred cats were overrepresented compared to the general hospital population. The aetiology of canine IVDD is considered 186 multifactorial with genetic, anatomical and biomechanical factors involved.<sup>18</sup> Developments 187 188 in the knowledge of canine IVDD have demonstrated an import role of genetic factors in the development of IVDD.<sup>19-21</sup> Identified genes are associated with the chondrodystrophic 189 phenotype, which is characterised by dogs with relative long spines and short limbs.<sup>19,20</sup> The 190 191 Dachshund, the dog breed most commonly affected by IVDD, is the prototype of such a 'long 192 and low' chondrodystrophic dog breed and this type of body conformation is indeed considered a major risk factor for the development of thoracolumbar IVDD.<sup>13</sup> The Persian and British 193

194 Shorthair are genetically related breeds with the Persian being the foundation breed of the 195 'Persian family members', which includes the British Shorthair, Scottish Fold, and Selkirk Rex. All these breeds share the brachycephalic structure of the head.<sup>22,23</sup> Although such breed 196 development strategies result in members of different, but closely related, breeds to share the 197 same general and genetic health concerns <sup>23</sup>, it remains currently unclear if a relationship exists 198 199 between the brachycephalic phenotype, other conformational changes, and ultimately, thoracolumbar IVDD. Alternatively, it cannot be excluded that the results of our study do not 200 201 reflect a true breed predisposition, but rather the willingness of owners of financially more 202 valuable purebred cats to seek referral for advanced diagnostic procedures.

In agreement with previous findings <sup>9</sup>, cats with thoracolumbar IVDD were generally old with most affected cats being 8 years or older. The results of this study however demonstrated that affected purebred cats were significantly younger than non-purebred cats. Although this age difference can be considered an illustration of their presumed predisposition for thoracolumbar IVDD, it cannot be excluded this finding represents again an increased willingness of owners to seek referral and pursue expensive diagnostic evaluations in relative younger cats.

In agreement with previous studies <sup>5,9</sup>, two types of thoracolumbar intervertebral disc 209 210 herniation were seen in affected cats; IVDE and IVDP. Intervertebral disc extrusions are 211 characterised by herniation of degenerated and calcified nucleus pulposus through a fully ruptured anulus fibrosus, while IVDP is characterised by a focal and more gradual extension 212 of the anulus fibrosus into the vertebral canal.<sup>18</sup> Although similar histopathological 213 abnormalities are seen in both types of intervertebral disc herniation <sup>24</sup>, IVDE and IVDP are 214 associated with different clinical characteristics in dogs.<sup>14,15,25</sup> Intervertebral disc extrusions 215 216 are typically associated with an acute onset of severe neurological signs, while dogs with IVDP typically present with milder clinical signs and a chronic, progressive clinical history.<sup>14,15,25</sup> In 217 218 agreement with these findings, cats with IVDE and IVDP demonstrated differences in their 219 clinical presentation. Cats with IVDE had a shorter duration of clinical signs before 220 presentation and had more severe neurological deficits compared to cats with IVDP. These 221 differences are not surprising and most likely reflect the pathophysiological differences 222 between both types of IVDD. Intervertebral disc extrusions are characterised by a sudden 223 extrusion of calcified and fragmented nucleus pulposus, which results in both contusion and compression of the spinal cord.<sup>26</sup> It is therefore not surprising that affected cats typically 224 demonstrated an acute onset of severe spinal cord dysfunction. In contrast, IVDP is typically 225 226 associated with gradual spinal cord compression without contusion. Affected cats therefore 227 typically presented with a more gradual onset of milder clinical signs.

228

#### 229 Conclusions

Thoracolumbar IVDD should be considered an uncommon disease in cats. Its prevalence is however higher in purebred cats, especially Persians and British Shorthairs. Further studies are necessary to evaluate if this finding represents a true breed predisposition or an increased willingness to pursue advanced diagnostics in financially more valuable pedigree cats. Two types of intervertebral disc herniations, IVDE and IVDP, occur in cats. In agreement with findings in dogs, cats with IVDE present with a shorter duration of clinical signs and milder neurological deficits compared to cats with IVDP.

237

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242 or not-for-profit sectors.

#### 243 Conflict of Interest

244 The authors do not have any potential conflicts of interest to declare.

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# 314 **Figure Legends**

**Table 1.** Breed distribution of 31 cats diagnosed with thoracolumbar intervertebral disc

## 316 disease

Affected breed	Number of cats
Domestic shorthair	9
Domestic longhair	5
British Shorthair	5
Persian	4
Bengal	2
Siamese	2
Havana Brown	1
Maine Coon	1
Sphynx	1
American Shorthair	1