

1 **Use of clinical vignette questionnaires to investigate the variation in management of**
2 **keratoconjunctivitis sicca and acute glaucoma in dogs**

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16
17 **Abstract**

18
19 There is little peer-reviewed research assessing therapeutic effectiveness in canine eye disease.
20 Current treatments used in first opinion and ophthalmology referral practices are also somewhat
21 poorly documented. The aim of this study was to investigate the current management of canine
22 keratoconjunctivitis sicca (KCS) and acute primary angle-closure glaucoma (PACG) by veterinary
23 surgeons. Questionnaires using clinical vignettes were administered to a cross section of general
24 practitioners ('GPs') and veterinarians engaged in or training for postgraduate ophthalmology
25 practice ('PGs'). Similar treatment recommendations for KCS (topical cyclosporine, lubricant,
26 antibiotic) were given by both groups of veterinarians with the single exception of increased topical
27 antibiotic use by GPs. Treatment of acute glaucoma diverged between groups: PGs were much more
28 likely to recommend topical prostaglandin analogues (PGAs) and a wider array of both topical and
29 systemic treatments were recommended by both groups. Systemic ocular hypotensive agents were
30 suggested infrequently. Our results suggest that treatments may vary substantially in ocular
31 conditions, particularly in conditions for which neither guidelines nor high quality evidence exists.
32 This study highlights the need for novel strategies to address evidence gaps in veterinary medicine,
33 as well as for better evaluation and dissemination of current treatment experience.

34
35 **Introduction**

36
37 Keratoconjunctivitis sicca (KCS) and acute angle-closure glaucoma (PACG) can cause significant
38 disability in dogs (Chester and Clark, 1987). Incidence and prevalence data for each is not well
39 established but risks appear to be higher in some breeds and with increasing age (Gelatt and
40 MacKay, 2004a; Sanchez and others, 2007). Veterinarians routinely encounter these and other
41 clinical conditions for which there is limited evidence available to guide clinical decision making.

42 Currently there is only one veterinary pharmaceutical approved for the treatment of KCS and none
43 for the treatment of glaucoma; it is unknown how this may affect treatment choice but could
44 potentially result in diverse management strategies.

45

46 Numerous clinical guidelines have been developed for the treatment of human disease, in part to
47 address unwanted treatment variation and to improve quality of care (Timmermans and Mauck,
48 2005). In medicine, greater treatment variation is seen for interventions which have uncertain or
49 marginal benefit and for conditions which lack clinical guidelines (Skinner, 2011). Veterinary
50 guidelines rely more heavily on consensus due to a small evidentiary base but areas with greater
51 treatment uncertainty are argued to be most needful of guidance (Polzin and Cowgill, 2013). While
52 guidelines and consensus statements now exist for a number of companion animal conditions (e.g.
53 Atkins and others, 2009; Podell and others, 2016; Olivry and others, 2010), we are unaware of any
54 clinical guidelines for canine ophthalmic disease.

55

56 Clinical vignette-based questionnaires are a useful way of assessing treatment patterns and variation
57 in clinical practice; they have been used to assess adherence to guidelines and to assess factors in
58 clinical decision-making in medicine (Peabody and others, 2004; Veloski and others, 2005).

59 Additionally, vignettes have been combined with Delphi methodology to achieve expert consensus in
60 optimizing treatment, as well as in establishing evidence gaps (Rose and Kagan, 1998). Use of open,
61 rather than closed, questions in vignettes has been reported to better describe clinicians' actual
62 practice patterns (Pham and others, 2009) and provide insight into what is accepted current
63 practice.

64

65 The aim of this study was to survey veterinarians about the current management of KCS and acute
66 glaucoma. Additionally, we aimed to explore the variation in treatment amongst all veterinarians
67 and between general practitioners and veterinarians with postgraduate training in ophthalmology.

68

69 **Materials and methods**

70

71 **Sampling and data collection**

72 The target population was all members of the veterinary profession in the UK. The sampling frames
73 were a convenience sample of veterinarians on a mailing list held by the Centre for Evidence-based
74 Veterinary Medicine (CEVM) (identified from another survey initially approaching respondents using
75 a list of RCVS members who were willing to be contacted, Nielsen and others, 2014), and attendees
76 at the British Association of Veterinary Ophthalmologists (BrAVO) Winter conference (2011).

77

78 A questionnaire (Appendix 1) was constructed consisting of 22 open and closed-end questions across
79 five sections as part of a student research project (Corinne Wigfall). These sections covered the
80 diagnostic tools used for ophthalmological cases, the sources of information accessed by vets and
81 factors considered in clinical decision-making for ocular conditions, as well as questions relating to
82 respondent demographics (age, gender, year of graduation, ophthalmology postgraduate
83 certification or training). The additional two sections presented two clinical vignettes—the first
84 based on a West Highland White Terrier with KCS and the second a Cocker Spaniel presenting with
85 acute PACG. After each vignette, veterinarians were asked what treatments, additional
86 investigations, long term management and recheck advice they would give for each case. The design

87 of the vignettes was based on “textbook” cases to minimize diagnostic confusion while the
88 associated questions were derived from a similar survey undertaken by Davies (2015). The
89 questionnaire was pre-tested by 20 people, and piloted by eight veterinarians and three non-
90 clinicians.

91

92 An online questionnaire was constructed and administered through cloud-based software
93 (SurveyMonkey Inc., California, USA) to the CEVM mailing list. Online respondents were
94 encouraged to fill out the questionnaire by being entered into a prize draw for a £50 gift;
95 respondents were anonymized for analysis. The online survey was initiated October 26, 2011 and
96 closed November 18, 2011. A first reminder was sent 2 weeks after the initial email followed by a
97 final reminder two days before survey close. Paper questionnaires identical in sequence and content
98 to the online questionnaire were distributed to the attendees during one day of the British
99 Association of Veterinary Ophthalmologists Winter conference and were collected back by three of
100 the authors at the end of the day (November 5, 2011).

101

102 Ethical approval for the study was received from the ethics committee at the School of Veterinary
103 Medicine and Science at The University of Nottingham.

104

105 Data management and analysis

106 Returned online responses were downloaded to Microsoft Excel V.14.0.6 (2010 Microsoft
107 Corporation) whilst paper questionnaire responses were manually entered into the same
108 spreadsheet. Data relating to proposed treatments and diagnostic investigations were extracted
109 from open ended responses by one coder (Constance White) and categorically classified into generic
110 drug name and/or category, surgical or procedural interventions, diagnostic test, and other patient
111 assessments. Data relating to long term recommendations were extracted by one coder (Constance
112 White) and classified into categories relating to prognosis, salvage treatment options, chronicity, and
113 owner communication/compliance. Suggested reevaluation times were converted from text to
114 numerals and where ranges were given, mean time calculated.

115

116 Statistical analysis was performed with a commercially available statistical package (Stata IC13).
117 Continuous data (age, years since graduation, recheck intervals) were assessed for normality by the
118 Shapiro-Wilk normality test and were subsequently analyzed using Mann-Whitney U tests. Chi-
119 square tests were used to compare categorical data between groups except when expected cell
120 counts were ≤ 5 , where the more conservative Fisher’s exact test was used. Not all respondents
121 answered all questions; proportions are calculated using the total numbers of respondents
122 completing each question unless otherwise indicated. Statistical significance was set at the 0.05
123 level; when multiple comparisons were undertaken, p values were adjusted for significance at this
124 level with the Dunn-Bonferroni method (Pagano and others, 2009). In brief, for a p value to reach
125 significance with correction for multiple comparisons, value must be $<0.05/k$ where k is the number
126 of comparisons. Significant p values are reported in text when not included in tables.

127

128

129 **Results**

130

131 Response rate

132 Of 1421 successful email invitations, 490 (34.5%) online questionnaires were returned. Of those,
 133 392 were from veterinarians engaged in small animal practice. Sixty one paper questionnaires were
 134 returned by British Veterinary Ophthalmologist Association (BrAVO) conference attendees (total
 135 number of conference attendees unknown). Of the total number of eligible responses (453), 70
 136 were engaged in or training for postgraduate ophthalmology practice; from here on known as 'PGs')
 137 while 383 were engaged in general practice (from here on known as 'GPs'). Not all 453 respondents
 138 answered all questions within the questionnaire (Table 1).

139

140 Table 1 Demographic and vignette question response rate. KCS = Keratoconjunctivitis sicca

141

	Overall n	Overall %	GP n	GP %	PG n	PG %
Survey	453	100	383	100	70	100
Age	330	72.8	260	67.9	70	100
Gender	332	73.3	262	68.4	70	100
Graduation year	331	73.1	261	68.1	70	100
KCS treatment	399	88.1	329	85.9	70	100
Further investigation KCS	395	87.2	195	50.9	53	75.7
KCS diagnostics	252	55.6	197	51.4	55	78.6
KCS recheck interval	396	87.4	326	85.1	70	100
KCS long term management	334	73.7	266	69.5	68	97.1
Glaucoma treatment	330	72.8	260	67.9	70	100
Glaucoma further investigation	323	71.3	254	66.3	69	98.6
Glaucoma diagnostics	260	57.4	191	50.0	69	98.6
Glaucoma recheck interval	259	57.2	206	53.8	53	75.7
Glaucoma long term management	262	57.8	194	50.6	68	97.1

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144 Respondent characteristics

145 Sixty three percent of all respondents were female, with a somewhat higher proportion of males in
 146 the PG group, a difference which did not reach statistical significance. Overall median age of
 147 respondents was 37 years, with PGs significantly older than the GP group. Median year of
 148 qualification was significantly earlier for PGs than for GPs. Analysis stratified by gender did not
 149 eliminate age or year of qualification differences between PGs and GPs (Table 2). When participants
 150 were de-anonymized by email address subsequent to analysis, credentials and practice type could be
 151 ascertained for 41 of the 70 PG respondents. Of those, eight were RCVS Specialists in
 152 ophthalmology, 28 were designated ophthalmology certificate holders (26/28 CertVOphthal), four
 153 were ophthalmology certificate candidates, and one was a non-identified certificate candidate.
 154 Overall, 88% (36/41) of those successfully de-anonymized were in referral practice at the time of the
 155 survey.

156

157 Table 2 Participant responses to demographic questions, comparison between practitioner groups

	Overall n	Overall	GP n	GP	PG n	PG	p value
Gender							
Male	123	37.0%	91	34.7%	32	45.7%	0.091
Female	209	63.0%	171	65.3%	38	54.3%	
No answer given	121		121		0		

Age							
Median age (all)	330	37.0	260	35.5 years	70	42.0 years	*0.0002
Median age (male)	123	41.0	91	40.0 years	32	45.5 years	*0.0212
Median age (female)	206	35.0	168	33.0 years	38	38.5 years	*0.0036
No answer given	123		124		0		
Year of qualification							
Median year qualified (all)	331	1998	261	2001	70	1995	*0.0001
Median year qualified (male)	123	1995	91	1996	32	1989	*0.0093
Median year qualified (female)	207	2001	169	2002	38	1998	*0.0055
No answer given	122		122		0		

158 Categorical data chi square test. Continuous data Mann-Whitney test

159 ***Significant with Bonferroni corrected p <0.05**

160

161

162 Keratoconjunctivitis sicca

163 Initial KCS treatment recommendations were offered by 399 respondents. Six different topical
 164 treatments were nominated (Table 3). The majority of both groups recommended cyclosporine
 165 (CSA) and an ocular lubricant. However, a significantly larger portion of GPs suggested using topical
 166 antibiotics.

167

168 Most respondents suggested a combination of topical therapies; a wider range of combinations
 169 were offered by GPs (GPs 12 combinations, PGs 8 combinations). A majority (98%) of respondents
 170 suggested one of eight different combinations of the four most common topicals (Figure 1). The top
 171 four combinations were recommended by 85.1% of GPs and 90.0% of PGs. PGs were significantly
 172 more likely to use topical CSA in combination with lubricant as sole treatment (chi square p=0.001)
 173 but no other significant differences were found. Amongst both groups, there were few
 174 recommendations of systemic therapies: 34 veterinarians recommended a systemic nonsteroidal
 175 anti-inflammatory (NSAID), eight veterinarians recommended systemic antibiotics, and one
 176 recommended systemic steroids for initial treatment.

177

178 Of 395 veterinarians who considered whether further investigation of KCS was warranted, a majority
 179 (63.8%) recommended further diagnostic tests (Figure 2). The most common suggestion was
 180 fluorescein staining. PGs were significantly more likely to recommend culture, tear film breakup
 181 testing, slit lamp evaluation, and Rose Bengal staining when compared to GPs (p<0.003 for each
 182 item, Fisher's exact test). Small numbers of respondents (<12 per recommendation) suggested
 183 evaluation for drug history, atopic dermatitis, and neurogenic causes of dry eye. Suggested recheck
 184 intervals differed significantly between GPs and PGs. Median time suggested for first recheck was 7
 185 days (range 2-52, IQR 7-14 days) for GPs versus a median of 14 days (range 5-60, IQR 12-28 days) for
 186 PGs (Mann Whitney U p=0.0000).

187

188 More than 40% of both groups discussed the need for long term therapy and regular assessment.
 189 Although the questionnaire did not solicit recommendations for refractory disease, multiple
 190 respondents offered suggestions in case of treatment failure: twelve individuals recommended
 191 compounded cyclosporine ophthalmic suspension while six suggested tacrolimus. Parotid duct
 192 transposition was considered by ten respondents in each group.

193

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195
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Table 3 Topical treatment recommendations for KCS by participants. NSAID = Nonsteroidal anti-inflammatory drug

Treatments	Overall n	Overall %	GP n	GP %	PG n	PG %	p value
Cyclosporine	371	93.0	304	92.4	67	95.7	0.324
Lubricant or tear replacement	319	78.0	256	77.8	63	90.0	0.021
Antibiotic	277	69.4	239	72.6	38	54.3	*0.002
Steroid	58	14.5	44	13.4	14	20.0	0.153
Tacrolimus	2	0.5	0	0.0	2	2.9	‡0.030
Topical NSAID	1	0.25	0	0.0	1	1.4	‡0.175

197 ***Significant with Bonferroni corrected p <0.05, chi square test unless otherwise indicated**

198 ‡ Fisher's exact test

199
200

201 Acute Glaucoma

202 A total of 330 veterinarians made treatment recommendations for PACG. Half of all GPs indicated a
203 desire to refer the glaucoma patient acutely but many of those also suggested some initial
204 treatments. Ten topical agents for PACG management were nominated (Table 4). Of those, PGs
205 were significantly more likely to recommend a prostaglandin analogue (PGA) and steroid. GPs
206 suggested the use of pilocarpine significantly more often than PGs. Respondents who suggested
207 pilocarpine were not significantly different in age (Mann Whitney U p=0.5989), years of qualification
208 (Mann Whitney U p=0.8615), or gender from other veterinarians (chi square p=0.428). There were
209 small but significant differences in choice of CAI and PGA agents selected, with a greater fraction of
210 PGs suggesting brinzolamide and travoprost.

211

212 Nineteen combinations of the five most commonly suggested topicals were recommended by
213 respondents (GPs 18 combinations, PGs 10 combinations). The ten most common combinations
214 were suggested by 72.6% of GPs and 95.7% of PGs (Figure 3). The top four combinations were
215 recommended by 55.3% of GPs and 77.2% of PGs. More than half (52.9%) of PGs chose a PGA
216 (typically latanoprost or travoprost) in combination with a carbonic anhydrase inhibitor (CAI;
217 predominately dorzolamide), with or without additional timolol and/or topical steroid. GPs
218 nominated PGAs significantly less often and were more likely to suggest a CAI alone or in
219 combination with topicals other than PGAs. Fewer GPs suggested CAI in fixed combination with
220 timolol (GPs 15 of 148 CAI suggestions, PGs 13 of 50 CAI suggestions, chi square p=0.001).

221

222 Many systemic therapies were also recommended (Table 5). Analgesic or anti-inflammatory drugs
223 were suggested by a large proportion, with NSAIDs most frequently specified. Twenty individuals
224 used a combination of products. Small numbers of respondents recommended systemic mannitol or
225 CAI to reduce intraocular pressure (IOP). A handful of respondents recommended antihypertensive
226 or diuretic drugs. No significant differences were found between GPs and PGs in their
227 recommendations for systemic agents.

228

229 Of the 260 respondents who answered questions about further investigations, the majority (79.0%)
230 recommended further diagnostics but few GPs made specific diagnostic recommendations (Figure

231 4). PGs suggested gonioscopy, slit lamp evaluation, ocular ultrasound, and Schirmer tear testing at
 232 significantly greater rates than GPs (chi square $p < 0.001$ for each test). After adjustment for access to
 233 a gonioscopy lens, PGs were still significantly more likely to recommend gonioscopy (chi square
 234 $p = 0.000$). Specific assessment for uveitis ($n = 7$), lens luxation ($n = 27$), and vision ($n = 7$) were
 235 recommended by a minority of each group. A significantly higher proportion of PGs recommended
 236 evaluation of the contralateral eye (3.1% GPs, 27.5% PGs, chi square $p = 0.000$).

237
 238 Suggested recheck intervals did not significantly differ between GPs and PGs. Median time
 239 suggested for first recheck was 1.5 days (range 1-14, IQR 1-3 days) for GPs versus a median of 2 days
 240 (range 0.6-7, IQR 1-3.5 days) for PGs. More than a third of PGs ($n = 25$) recommended hospitalization
 241 until IOP normalized, a significantly greater proportion than GPs ($n = 12$, chi square $p < 0.001$).

242
 243 Of the 262 respondents who gave long term management recommendations, PGs and GPs were
 244 equally likely to discuss the need for ongoing treatment of glaucoma (11.9% GPs, 17.9% PGs), regular
 245 monitoring (30.4 % GPs, 36.2% PGs), and long term prognosis (13.4% GPs, 20.3% PGs). More than
 246 half of PGs (56.5%) discussed evaluation, prognosis and/or prophylaxis of the contralateral eye,
 247 whilst significantly fewer GPs (23.7%) did so (chi square $p = 0.000$).

248
 249

250 Table 4 Topical treatment recommendations for acute glaucoma by participants. NSAID =
 251 Nonsteroidal anti-inflammatory drug

Treatments	Overall n	Overall %	GP n	GP %	PG n	PG %	p value
Carbonic anhydrase inhibitor	198	60.0	148	56.9	50	71.4	0.028
Dorzolamide	151	45.8	123	47.3	28	40.0	0.276
Brinzolamide	31	9.4	15	5.8	16	22.9	*0.000
Either	11	3.3	7	2.7	4	5.7	
Unspecified	5	1.5	3	1.2	2	2.8	
Prostaglandin analogue	128	38.8	72	27.7	56	80.0	*0.000
Latanoprost	81	24.5	53	20.4	28	40.0	*0.001
Travoprost	33	10.0	14	5.4	19	27.1	*0.000
Either	7	2.1	0	0	7	10.0	
Unspecified	7	2.1	5	1.9	2	2.9	
Timolol	41	12.4	27	10.4	14	20.0	0.030
Steroid	30	9.1	16	6.2	14	20.0	*0.000
Pilocarpine	30	9.1	30	11.5	0	0	*0.003
Atropine	13	4.0	13	5.0	0	0	‡0.078
NSAID (topical)	12	3.6	12	4.6	0	0	‡0.078
Antibiotic	10	3.0	9	3.5	1	1.4	‡0.695
Lubricant	6	1.8	5	1.9	1	1.4	‡1.000
Iopidine	1	0.3	0	0	1	1.4	‡0.212

252 ***Significant with Bonferroni corrected $p < 0.05$, chi square test unless otherwise indicated**

253 ‡ Fisher's exact test

254

255

256 Table 5 Systemic glaucoma therapies suggested by participants. NSAID = Nonsteroidal anti-
 257 inflammatory drug; IOP = Intraocular pressure; IV = Intravenous; CAI = Carbonic Anhydrase Inhibitor;
 258 ACE = Angiotensin Converting Enzyme

Treatments	Overall n	Overall %	GP n	GP %	PG n	PG %	p value
<i>Pain/antiinflammatory</i>							
NSAID	155	47.0	118	45.4	37	52.9	0.266
Unspecified analgesia	25	7.6	24	9.2	1	1.4	‡0.038
Opioid or tramadol	19	5.8	10	3.8	9	12.9	*0.004
Glucocorticoid	4	1.2	3	1.2	1	1.4	‡1.000
All pain/antiinflammatory	183	55.5	144	55.3	39	55.7	0.961
<i>IOP agents</i>							
IV mannitol	34	10.3	26	10.0	8	11.4	0.727
Oral CAI	17	5.2	16	6.2	1	1.4	‡0.137
<i>Hypotensives/diuretics</i>							
Amlodipine	2	0.6	0	0.0	2	2.9	‡0.044
ACE inhibitor	1	0.3	1	0.4	0	0.0	‡1.000
Furosemide	4	1.2	4	1.5	0	0.0	‡0.582
<i>Referral</i>	133	40.3	130	50.0	3	4.3	*0.000

259 ***significant with Bonferroni corrected p<0.05, chi square test unless otherwise indicated**

260 ‡ Fisher's exact test

261

262

263 **Discussion**

264

265 Prior work has established that substantial treatment variation may occur in the management of
 266 canine diabetes and heart failure (Davies and others, 2015; Sinclair and others, 2014). This study
 267 demonstrates similar variation, particularly in the treatment of PACG. We speculate that this
 268 variation may be driven by knowledge gaps influenced by one or more of the following factors: lack
 269 of evidence-based and/or consensus guidelines, access to information, or differences in caseload
 270 and/or practice setting.

271

272 For KCS, fairly robust evidence (grade I, Roudebush and others, 2004) exists for topical CSA efficacy
 273 in prospective clinical trials and an approved veterinary ophthalmic preparation has been available
 274 for more than two decades (Kaswan and others, 1989; Morgan and Abrams, 1991; Olivero and
 275 others, 1991; Sansom and others, 1995). Frequent nomination of CSA for KCS treatment likely
 276 reflects acceptance of efficacy and incorporation into standards of care. The preference for CSA
 277 over tacrolimus may be driven by CSA's availability as a licensed veterinary product as well as
 278 current evidence which suggests equal efficacy of CSA and tacrolimus for treatment-naïve KCS
 279 (Berdoulay and others, 2005, Hendrix and others, 2011). Similarly, there was general agreement in
 280 favour of topical lubricant. Prior to the introduction of CSA, lubricants were the mainstay of KCS
 281 medical therapy (Blogg, 1980) and, extrapolating from human dry eye, may be reasonably expected
 282 to provide some symptomatic relief and corneal protection (Alves and others, 2013).

283

284 Apart from CSA, most topicals used in KCS have limited published evidence for efficacy and this may
 285 account for wider variation in their recommended use. There is sparse data regarding the

286 prevalence of secondary infection with conflicting recommendations for antibiotic use in KCS
287 (Giuliano and Moore, 2007; Maggs and others, 2012; Martin, 2010; Petersen-Jones, 1997; Salisbury
288 and others, 1995). Topical steroids are suggested by some veterinary ophthalmologists to decrease
289 conjunctival inflammation, discomfort and corneal scarring in KCS (Giuliano and Moore, 2007).
290 Topical steroid recommendations appear to rely on clinician experience and possibly extrapolation
291 from the human literature which has shown benefit in dry eye (Messmer, 2015).

292

293 While broad general agreement was found for KCS management, treatment suggestions for PACG
294 were more varied. GPs nominated topical PGAs significantly less frequently than did PGs while use
295 of CAIs was more similar between the two groups. There is reasonable evidence (grade III,
296 Roudebush and others, 2004) for both PGA and CAI efficacy for IOP reduction in beagles with open-
297 angle glaucoma, with PGAs offering superior duration and magnitude of IOP reduction (Gelatt and
298 McKay, 2001a, 2001b, 2002, 2004b; Plummer and others, 2006). However, no clinical trials assessing
299 safety or efficacy of these agents alone or in combination have been reported for the more common
300 syndrome of PACG (reviewed by Maślanka, 2015a, 2015b). Topical PGAs are preferred over systemic
301 agents in achieving IOP reduction by some authors (Alario and others, 2015; Maślanka, 2015b), a
302 view that was paralleled by our results. Clinical uncertainty in recognizing PGA contraindications
303 (anterior lens luxation and uveitis) may account for the lower rate of GP recommendation.
304 However, other factors may play a role in differential recommendations: pilocarpine has similar
305 contraindications yet was recommended by a number of GPs. It is striking that no PG recommended
306 pilocarpine; veterinary ophthalmologists appear to discourage pilocarpine due to ocular irritation
307 and perceived superiority of other ocular hypotensives (Alario and others, 2015). Choice of topical
308 PGA and CAI also varied between GP and PG groups with the latter group nominating travoprost and
309 brinzolamide significantly more frequently. Reasons for product choice were not elicited in our
310 questionnaire and we are unaware of any comparative efficacy trials between dorzolamide and
311 brinzolamide, or between latanoprost and travoprost, in acute canine glaucoma; however,
312 brinzolamide is suggested to result in less ocular irritation relative to dorzolamide (Alario and others,
313 2015). Likewise, more PGs recommended a topical steroid. Although we did not elicit the clinical
314 reasoning behind treatment suggestions, steroids may have been recommended due to the putative
315 role of inflammation in both genesis and progression of PACG (Dees and others, 2014; Reilly and
316 others, 2005); steroids may exacerbate ocular hypertension in cats and dogs but the response may
317 vary by individual and with the concurrent use of PGA (Herring, Herring, and Ward, 2004; Gelatt and
318 McKay, 1998; Gosling and others, 2016; Kahane and others, 2016). However, we are unaware of any
319 studies assessing the use of steroids in PACG (apart from prophylaxis in unaffected but at-risk eyes).
320 As would be anticipated, PGs recommended a greater number of specific ophthalmic diagnostics.
321 GP suggestions for additional investigation generally agreed with PG recommendations when the
322 suggested test was inexpensive and did not require specialized equipment or expertise. In
323 particular, gonioscopy may be difficult to master without routine practice and we are not aware of
324 any readily available training resources for GPs.

325

326 Recheck intervals and judgement regarding natural history and prognosis of KCS and glaucoma were
327 generally concordant between both groups with one exception: recheck intervals for KCS were
328 significantly shorter for GPs than for PGs. Topical CSA typically lags 3-4 weeks for maximal increase
329 in tear production (Olivero and others, 1991, Samson and others, 1995). The shorter median
330 interval suggested by GPs may reflect severity differences in initial presentation, misunderstanding

331 of CSA pharmacodynamics, decreased clinical confidence, or a variety of other factors not captured
332 in this survey. Alternatively, GP versus PG clinic proximity may affect recheck intervals amenable to
333 clients; however, the similarity of suggested glaucoma recheck intervals between the two groups
334 argues against client convenience as a driving factor.

335

336 Veterinarians in primary practice are required to have proficiency in multiple domains and may have
337 limited access to literature unless affiliated with academic practice; availability of veterinary
338 ophthalmologist advice may also vary due to geographic, social network, and practice
339 characteristics. Although management guides used by GPs uniformly recommend CSA and provide
340 algorithms for the treatment of KCS, most PACG references are less directive in treatment
341 recommendations and typically provide a more general pharmacologic review, with referral often
342 recommended as the preferred treatment strategy (Clode, 2015; Colitz, 2010; Reinstein and others,
343 2009). We speculate that the wider range of recommendations for PACG encountered amongst our
344 GP respondents may reflect a lack of clear and concise treatment guidelines for this condition;
345 guidance which may be particularly needed for cases which cannot be referred. PGs in this survey
346 also varied in their treatment recommendations, particularly with respect to the use of
347 combinations of topical agents; variable use of steroids and antibiotics in the case of KCS, as well as
348 agents combined with PGAs in PACG, suggest treatment uncertainties which may need additional
349 data to resolve. We suggest that establishing current practice in treating companion animal ocular
350 disease may at least allow for benchmarking of individual practitioners against their colleagues.
351 Additionally, these surveys can both highlight clinical questions of high priority and identify areas
352 needful of consensus guidance when evidence is lacking. We suggest incorporation of Delphi or
353 similar anonymized methods in formulating veterinary ophthalmology guidelines (Jones and Hunter,
354 1995). Adherence, credibility, and feasibility of consensus guidelines is suggested to improve when
355 general practitioners are included on consensus panels (Allan et al., 2015; Carlsen, Glenton, and
356 Pope, 2007; Carlsen and Norheim, 2008; Rashidian, Eccles, and Russell, 2008). Assemblage of
357 electronic cohort data from both referral and first opinion practices, as well as consideration of
358 multi-centre pragmatic clinical trials, may be cost-effective paths to generating better and externally
359 valid evidence.

360

361 Study limitations

362 This survey was distributed to a subset of RCVS registered veterinarians who had expressed
363 willingness to be contacted by the CEVM, as well as to attendees at an ophthalmology meeting.
364 Additionally, although the majority of respondents completed the survey via a web-based
365 instrument, questionnaire format (paper versus web-based) may have resulted in qualitative or
366 quantitative differences in responses. Several levels of self-selection bias may have been
367 introduced: veterinarians who were willing to be contacted may have a greater interest in evidence-
368 based medicine while veterinarians who responded to the web-based survey may have better access
369 or understanding of a web-based instruments. Respondents were more likely to be female and
370 newer graduates than RCVS members in total; a contemporary survey of RCVS members found a
371 median qualification year of 1991, with approximate gender parity in registered members
372 (Robertson-Smith and others, 2010). As with any vignette-based survey, conformity of
373 recommendations to actual practice cannot be established.

374

375 Conclusion

376 This survey of veterinarians in the United Kingdom found variation in the treatment of KCS and PACG
377 between practitioners. Variation in management may be driven by a limited evidence base, lack of
378 clinical guidelines, heterogeneous training and practice settings, and clinical confidence or interest
379 on the part of respondents. Additionally, greater treatment variation was found in management of
380 PACG, a condition for which no approved veterinary products are available. Further work is needed
381 in assessing factors responsible for treatment variation and in optimizing resources and strategies
382 for building and disseminating evidence-graded, relevant diagnostic and treatment
383 recommendations to practitioners.

384

385

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392

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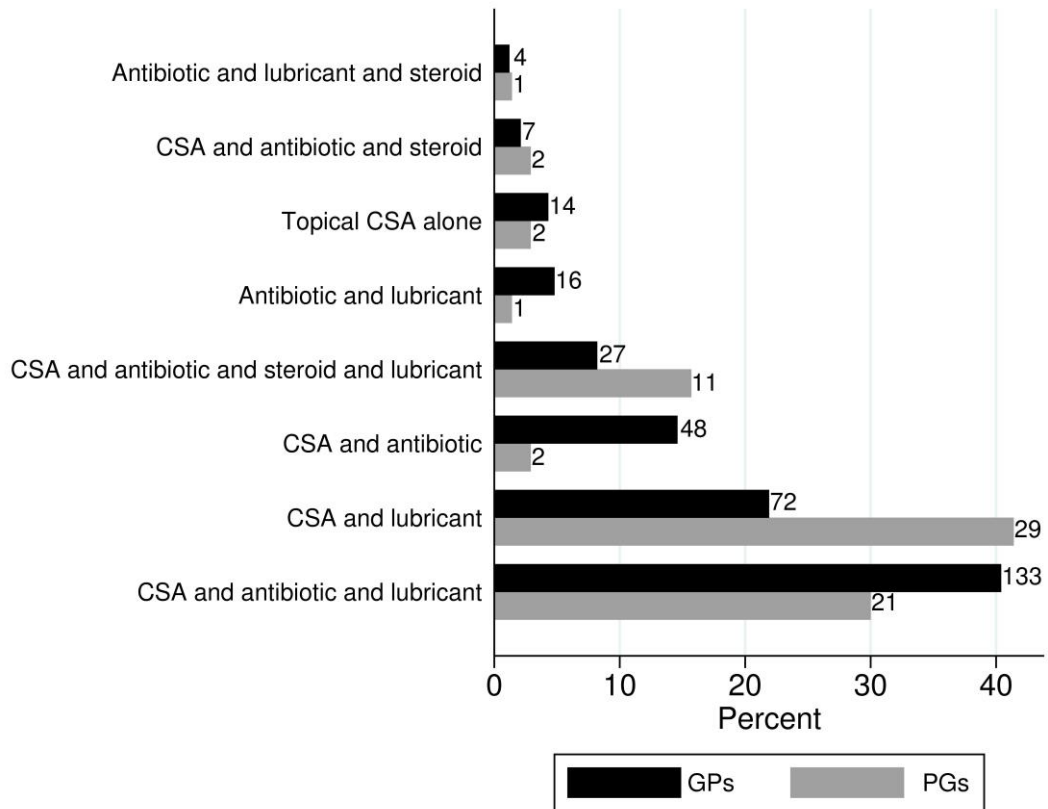
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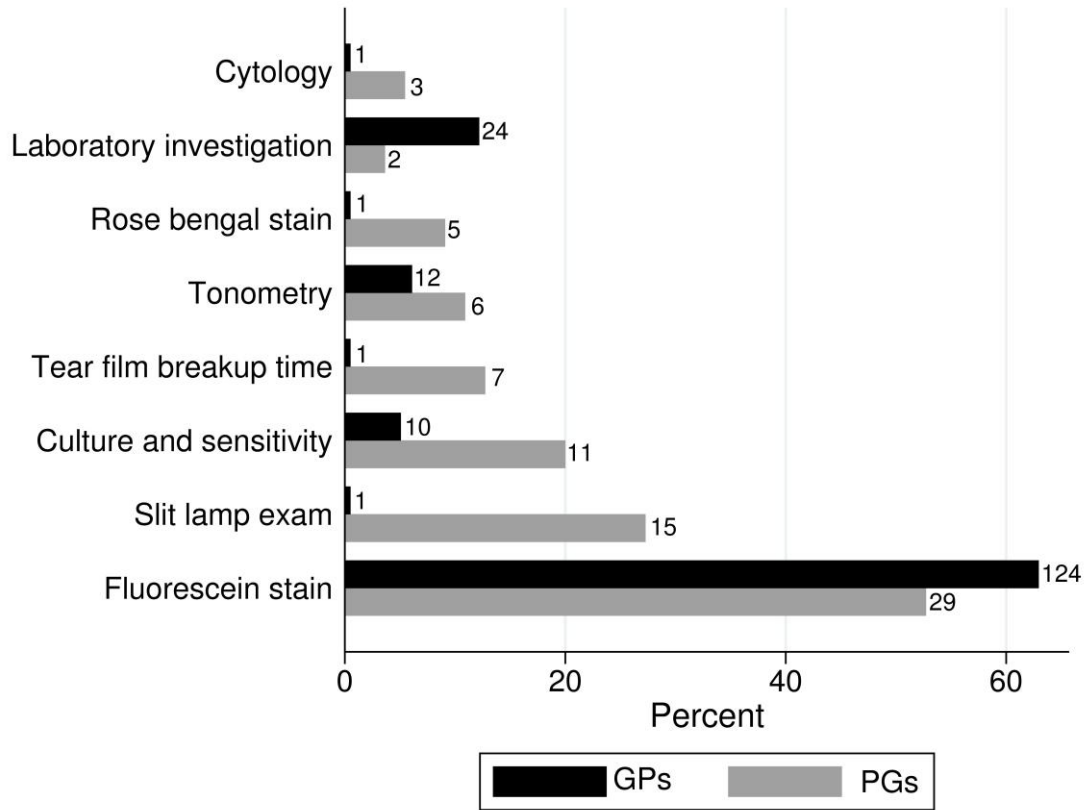
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538 **Figure 1**
 539 Eight most common recommended topical treatment combinations for KCS (numbers indicate
 540 number of respondents nominating that combination, percentage of total respondents
 541 recommending KCS treatments was 330 GPs, 70 PGs)



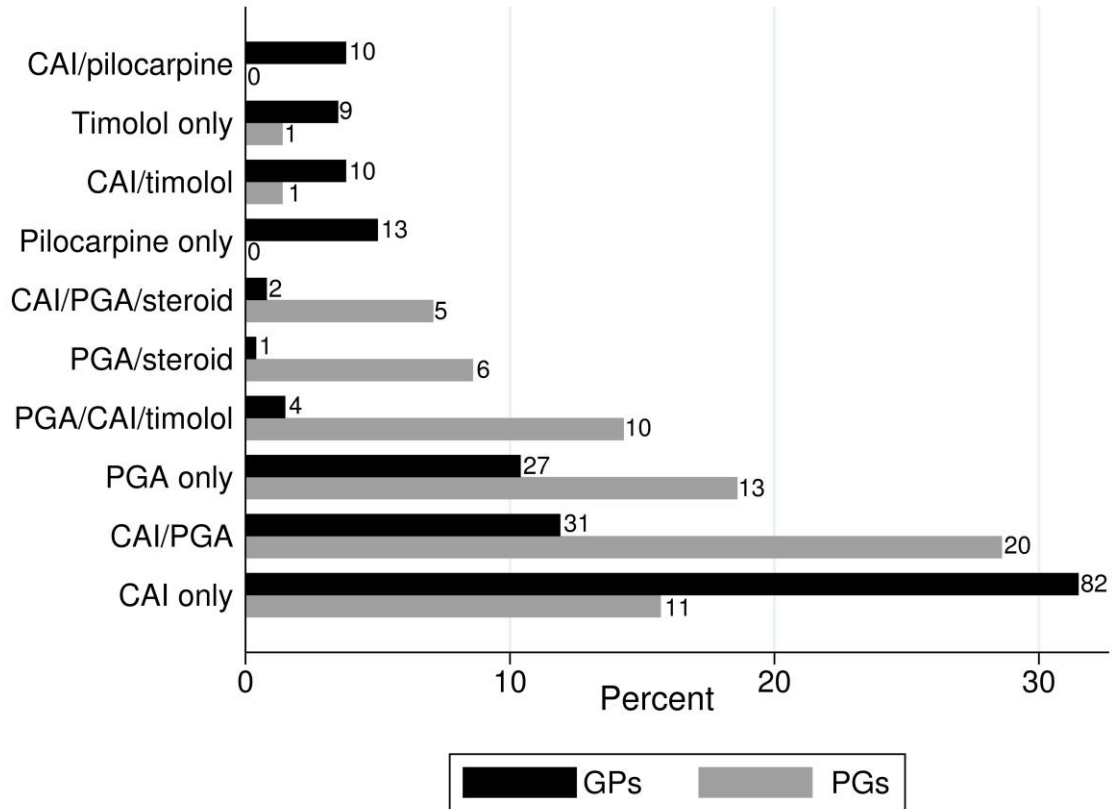
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544 **Figure 2**
 545 Additional diagnostic tests recommended by those who suggested further evaluation for KCS
 546 (numbers indicate number of respondents nominating that diagnostic test, percentage of total
 547 respondents recommending KCS diagnostics was 197 GPs, 55 PGs)



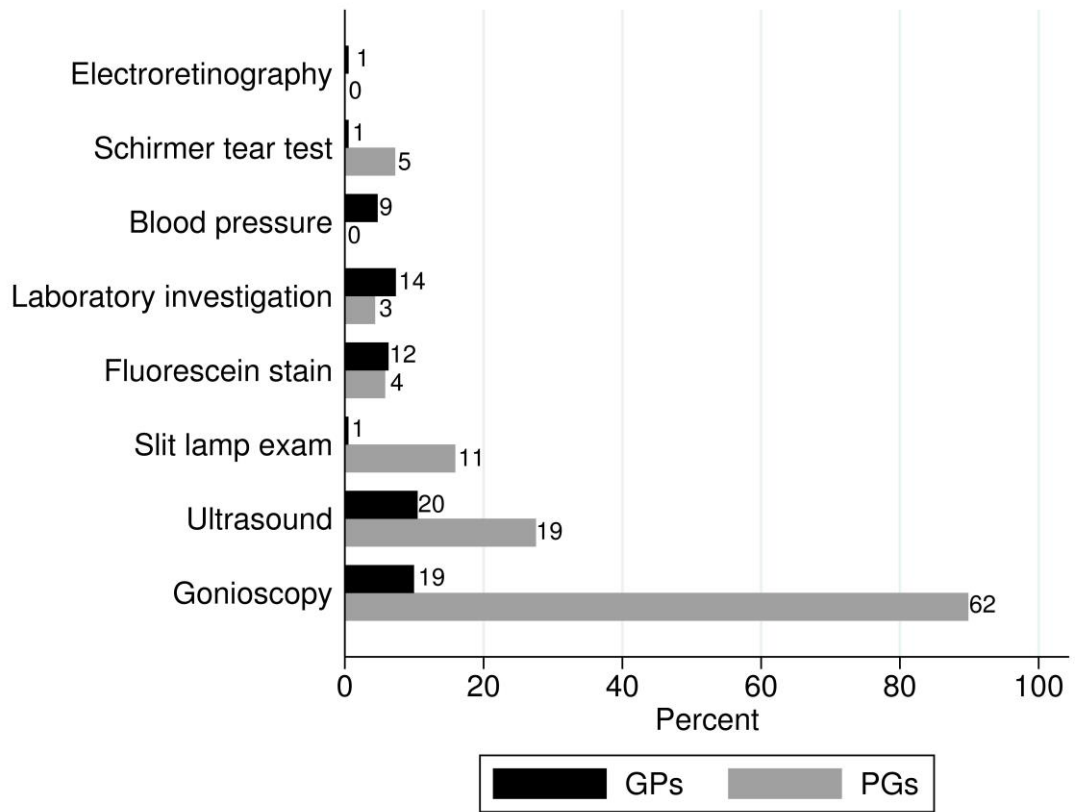
548

549 **Figure 3**
 550 Most common recommended topical treatment combinations for glaucoma (CAI = topical carbonic
 551 anhydrase inhibitor; PGA = prostaglandin analog, (numbers indicate number of respondents
 552 recommending that glaucoma treatment, percentage of total respondents recommending KCS
 553 diagnostics was 260 GPs, 70 PGs)



554
 555
 556

557 **Figure 4**
558 Additional diagnostic tests recommended by those who suggested further evaluation for glaucoma
559 (numbers indicate number of respondents nominating that diagnostic test, percentage of total
560 respondents recommending glaucoma diagnostics was 191 GPs, 69 PGs)



561
562