1 **Management and horse-level risk factors for recurrent colic in the UK general**
2 **equine practice population**

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9 **Summary**

10 **Reasons for performing study:** Recurrent colic occurs frequently in the general
11 horse population but little evidence exists about what factors place horses at greater
12 risk of recurrent colic.

13 **Aims:** To quantify time-varying and non time-varying risk factors for recurrent colic
14 among horses attended by first-opinion veterinary surgeons in NW England.

15 **Methods:** A nested case –control study was conducted on data from a prospective
16 longitudinal cohort study of 127 horses recruited subsequent to an episode of
17 medical colic. Data were collected on management and recurrent colic episodes at 4
18 monthly intervals by telephone questionnaires. All recurrent colic episodes were
19 selected as cases; controls were unmatched and randomly selected from all horse
20 time at risk. Data relating to the 30 days prior to the date of colic or control selection
21 were used to determine exposure status. Multivariable logistic regression analyses
22 were used to determine risk factors for recurrent colic.

23 **Results:** In total, 59 cases and 177 controls were included. The final model showed
24 that horses that displayed crib-biting/windsucking (CBWS) (OR 10.1, 95% CI 2.5,
25 41.0) or weaving behaviour (OR 3.9, 95% CI 1.5, 10.1) had an increased risk of
26 recurrence of colic. Increasing time at pasture reduced the risk of recurrence (OR
27 0.99, 95% CI 0.99, 1.0). A significant interaction was found suggesting the risk

28 associated with CBWS may be modified by feeding fruit/vegetables, however further
29 research is required before recommendations for feeding practices can be made.

30 **Conclusions and potential relevance:** This study suggests that sufficient access to
31 pasture may be an important means of reducing recurrent colic risk. The behavioural
32 risk factors highlight individuals who may be at increased risk of recurrent colic and
33 whose colic prevention strategies should be carefully managed.

34 **Introduction**

35 Colic is a high priority health concern for horse-owners [1]. It occurs frequently and
36 may result in the need for surgical intervention or the death of the horse [2, 3].

37 Whilst many colic cases are isolated episodes, recurrence is frequently reported
38 (following both medical and surgical colic episodes) and has been identified as a
39 frustrating problem to manage [4, 5]. In a previous study, the rate of recurrent colic
40 in the general horse population was shown to be high at 50 episodes of recurrence
41 per hundred horse-years-at-risk [6].

42 Previous epidemiological studies have identified factors associated with altered
43 likelihood of colic. These have included season and a number of management and
44 horse-level risk factors including; age and breed, crib-biting/windsucking (CBWS)
45 behaviour, parasites, dietary type and feeding practices, exercise, stabling and access
46 to pasture, access to water, transportation, vaccination, premises/owner factors and
47 use of the horse [7]. These findings highlight the multifactorial nature of colic and
48 horses that have suffered an initial colic episode have been shown to be at increased
49 risk of further colic episodes [8, 9, 10, and 11].

50 At present, there is little evidence available of horse and management level risk
51 factors associated with increased risk of recurrent colic. One study of horses seen by
52 ambulatory veterinarians in Texas compared horses with recurrent colic with two
53 control populations; horses with colic but no prior history of colic and horses without
54 colic (or prior history of colic) [12]. Risk factors associated with recurrent colic
55 were; previous abdominal surgery, age (> 8 years), feeding coastal grass hay, recent
56 change in diet, low stocking density (<0.5 horses/acre), geldings and the Arabian
57 breed. This study gave important indications of risk factors for recurrent colic,
58 although due to the retrospective case-control study format, it was not able to

59 investigate temporal (time-varying) relationships between the exposures (e.g.
60 management practices at that time) and risk of recurrent colic.

61 There is growing evidence to implicate a link between equine stereotypic behaviour
62 and increased colic risk. Studies investigating both epiploic foramen entrapment
63 colic [13] and Simple colonic obstruction and distention (SCOD) colic [11] found
64 increased risk if the horse displayed CBWS behaviour. The temperament of the
65 horse, especially if irritable and excitable has been suggested to be a risk factor for
66 colic [14]. 'Stress' has also been implicated in equine gastric ulceration syndrome
67 which may also present with chronic intermittent colic [15]. However, the link
68 between behaviour and colic is likely not straightforward as horses who were easily
69 frightened, excited, went off food when stressed or had an inquisitive nature were
70 found to be at reduced risk in one study [16]. Objective measures of what constitutes
71 'stress' in the horse and how this translates into colic risk are subjects worthy of
72 further research.

73 This study aimed to identify risk factors for recurrent colic (including those factors
74 which may vary over time) among the veterinary-accessing general horse population.
75 Hypotheses were that diet and management, particularly stabling, grazing and
76 exercise; preventive health care (such as anthelmintic treatment and dentistry) and
77 behavioural aspects influence the risk of recurrent colic.

78 **Materials and Methods**

79 *Study design and data collection*

80 A nested case-control design was used with cases and unmatched controls randomly
81 selected from a previously described longitudinal cohort study [6]. Both veterinary
82 attended (n=59) and owner reported (n=17) recurrent colic episodes were included.

83 In brief, the cohort study enrolled 127 horses recruited via first opinion equine
84 veterinary surgeons in the North West of UK. These were horses that were diagnosed
85 with colic and had responded to medical treatment. Clinical details of the recruitment
86 colic and each subsequent colic episode were sought from the attending veterinary
87 surgeon. Horses with a history of surgery for colic, those less than 6 months old and
88 mares with foals at foot were excluded from the study.

89 Owners completed a baseline and 3 follow up telephone questionnaires at
90 approximately 4 month intervals. The baseline questionnaire collected data on the
91 initial (recruitment) colic episode, the horses' signalment, use and behaviour,
92 prophylactic health care including vaccination, dentistry and deworming, and
93 management practices including diet, turnout and exercise routine.

94 The follow-up telephone questionnaires captured data that could potentially change
95 during the study period and recorded any further colic episodes. Information
96 regarding behaviour was not measured during follow-up, as it was considered that
97 this would change little over the course of the study. Participating owners were asked
98 to notify the study team if their horse had any further episodes of colic (including
99 any owner-reported colic episodes where a veterinary surgeon was not called). For
100 each recurrent colic episode, a further questionnaire was completed to ascertain: the
101 date of the colic, whether the recurrence satisfied the case definition, a description of
102 the colic, treatment and outcomes and whether the owner had any hypotheses of
103 cause and, what recommendations the attending veterinary surgeon had made.

104 Horses were censored if they died, had colic surgery or were lost to follow up. A
105 nested case-control study using data collected from this longitudinal cohort was
106 designed to analyse the effect of time-varying and non time-varying variables
107 occurring over the course of the study.

108 ***Case definition***

109 Recurrent colic was defined as an episode of colic diagnosed by a veterinary surgeon
110 or, behavioural signs of colic observed (in the case of owner reported colic), and
111 which occurred more than 48 hours after a prior episode of colic on the *proviso* that
112 the horse had been free from signs of colic, eating a normal diet and passing normal
113 faeces for a full 48 hours. Behavioural signs suggestive of colic included one or
114 more of the following signs; flank watching, pawing, kicking belly, rolling, violent
115 rolling, repeated stretching as if to urinate, grinding teeth, flehemen/curling lip,
116 sweating, flatulence, getting up and down/restless and other.

117 ***Selection of cases and controls***

118 Data were extracted from the cohort study and used to determine the effect of time-
119 varying and non time-varying variables occurring over the course of the year by
120 examining exposures in the 30 day period prior to being a case or control.

121 All recurrent colic episodes (total n=59 of which 17 were owner reported episodes)
122 were selected as cases and the data relating to 30 days prior to the colic episode were
123 used to determine exposure status. Three controls per case were randomly selected
124 from all horse-time at risk. All contributing time at risk was summated until the
125 point of loss to follow up, colic surgery or death due to colic or other reasons. Two
126 days from the recruitment episode, and 2 days subsequent to each episode of
127 recurrent colic were excluded from time at risk (according to our case definition).
128 Additionally, for each case of recurrent colic the 30 days prior to the colic could not
129 be selected as control data as these were contributory days to the 'case' time at risk
130 in line with other studies [11, 17].

131 From the remaining cumulative time at risk (44,301 days) [6] a list of computer
132 generated random numbers were used to select 177 control horse days. Case horses
133 could serve as controls before they became a case or when they were back 'at risk'
134 and a horse could be selected as a control at more than one time point. The selected
135 case and control days were transformed back into the corresponding dates for each
136 horse and exposure variables recorded within the 30 days prior to this date were
137 extracted.

138

139 *Statistical analysis*

140 Univariable analysis was conducted on all variables as listed in supplementary
141 information (see supplementary information tables 1 & 2). Categorical and
142 continuous variables were assessed using univariable logistic regression (Minitab
143 15). The functional form of the relationship between continuous variables and the
144 outcome were tested for linearity using Generalised additive models (GAM) [18] and
145 plotted using S-Plus 2000. In order to assess the effect of changes in management
146 that occurred during the study (i.e. time-varying effects) data were extracted and
147 recategorised. This included a change in: the time spent at pasture; the frequency of
148 forage feeds; the frequency of concentrate feeds; time spent exercising and a change
149 in stocking density between each of the follow up questionnaires. These variables

150 were recoded and defined categorically as follows: no change occurred, an overall
151 increase and an overall decrease between follow ups.

152 Prior to model building, all variables were assessed for correlation using Spearman's
153 correlation coefficients. Any variables with $p < 0.2$ were included in a multivariable
154 logistic regression model built manually using stepwise backwards elimination
155 (SPSS). Variables were retained if their exclusion resulted in a likelihood ratio test
156 statistic (LRTS) of $p < 0.05$ or if there was evidence of confounding. The resulting
157 model was retested by forcing all variables (with $p < 0.2$) back into the model. The
158 effect of biologically plausible interaction terms was tested in the model. Finally a
159 multi-level multivariable model was built incorporating a random effect term for
160 'horse' (as a number of horses had multiple colic events during the cohort) to assess
161 clustering within horse and the effect on the parameters of the model (MLwiN
162 Version 2.18 Centre for Multilevel Modelling, University of Bristol). Model fit was
163 assessed using the Hosmer-Lemeshow test statistic [19]. The stability of the model
164 and the influence of individual data points were explored by assessment of delta-beta
165 values for each variable in the final model. All other analysis except for multi-level
166 modelling was conducted in SPSS and Minitab.

167

168 **Results**

169 In total 59 recurrent colic episodes (including 17 owner reported episodes) and 177
170 controls were included. The median time to first episode of recurrence was 101 days
171 ($n = 43$, min 2, max 404, IQ range 217 days). Three horses had a first recurrence
172 within 7 days of the initial colic episode and seven horses had first recurrence within
173 30 days. There were 9 horses with 2 episodes of recurrence, 4 horses with 3
174 episodes, 2 horses with 4 episodes and 1 horse with 5 recurrent colic episodes during
175 the course of the cohort. For further details of horse-time contributed to study see
176 [6].

177 Tables 1 & 2 (within supplementary material) detail results of univariable analysis.
178 A total of 47 variables were used to build the multivariable model. A multivariable
179 logistic regression model (Table 1) showed that horses that displayed CBWS or
180 weaving behaviours, had reduced time spent at pasture and were fed probiotics had

181 an increased risk of colic. The variable “fed probiotics” was borderline significant
182 ($p=0.055$) and the overall fit of the model with the data was improved judging by the
183 Hosmer-Lemeshow test statistic hence it was retained within the model but should
184 be interpreted with caution.

185 Time spent at pasture (in hours per day per week) was found to approximate a linear
186 relationship with the risk of recurrence. Although the odds ratio was small (0.99) this
187 represents the change in risk of colic occurring per hour/day change in grazing over
188 the course of a week. For example, compared to a horse that is always stabled, a
189 horse with 12 hours/day/week access to pasture had almost half the risk ($OR=0.43$)
190 of recurrent colic (Table 2).

191 There was a significant interaction between feeding fruit/vegetables and CBWS
192 behaviour. This suggested that among horses that displayed CBWS behaviour, those
193 also fed fruit/vegetables were at reduced risk of recurrent colic ($OR = 0.15$)
194 compared to those that just demonstrated CBWS behaviour ($OR=10.1$) (see table 1
195 footnote).

196 A multilevel model, including horse as a random effect, showed there was no
197 significant within-horse clustering and hence no effect on the other parameters
198 within the model. Analysis of the delta beta distributions for the variables in the
199 model found that the CBWS variable had one influential data point (>0.4 or -0.4).
200 This was a control horse and its removal resulted in a larger odds ratio for risk of
201 CBWS (16.3, 95% CI 3.2, 82.4) in the model. The data for this horse were correct
202 and therefore were retained in the final analysis.

203 **Discussion**

204 This study has identified a number of factors associated with altered risk of recurrent
205 colic in the general horse population. Currently, there is little information on the
206 temporality of risk factors (i.e. changes that occur over time) and recurrent colic.
207 One study called for a ‘clearer definition of time relationships of events with colic’
208 in order that specific management recommendations could be made [8].

209 The use of a nested case-control design within a cohort study enabled particular
210 time-varying and non time-varying exposures to be examined. In contrast to many
211 previously published case-control studies on colic, the exposures were recorded

212 prospectively (i.e. prior to a horse having a recurrent colic episode). This creates
213 some logistical disadvantages as data collection is time consuming and involves
214 regular contact with participants throughout the study period, and losses to follow up
215 may occur more frequently due to the extended nature of the study (although our
216 participant retention rate was good 89.8%). However, these potential disadvantages
217 are outweighed by the benefits of obtaining likely better quality of data as recall bias
218 should be minimised. Using this type of study design, it was also possible to
219 examine a specific time period prior to the recurrent colic episode. The findings of
220 the present study builds upon those reported from the baseline survey [6] as it allows
221 for the variability that occurs within the management of the horse over the course of
222 a year and accounts for each individual episode of colic.

223 Horses that display CBWS behaviour have previously been shown to be at increased
224 risk of medical colic and some types of surgical colic lesions [6, 11, 17 & 20]. The
225 aetiology of this stereotypic behaviour is not fully understood and many hypotheses
226 have been proposed including confinement within a stable [21], reduced access to
227 pasture along with high concentrate and low forage diets [22], horse temperament,
228 other stressors, genetics or a form of gastrointestinal dysfunction [17 & 23]. CBWS
229 may not only be a marker for particular individuals that are prone to colic, it may
230 have a direct physical influence upon colic aetiology or could be a proxy for other
231 management factors involved in colic risk. Ultimately the link between CBWS
232 behaviour and colic remains unclear and warrants further investigation.

233

234 This study is the first to report an association between weaving behaviour and
235 increased risk of recurrent colic. Eleven (8.7%) horses among the cohort displayed
236 this form of behaviour, 7 of which had a colic recurrence (63.6% of horses that
237 weaved). Whereas CBWS behaviours are oral stereotypies, weaving is classed as a
238 locomotor stereotypy and is likely to have different predisposing causes. Hypotheses
239 of why horses may develop this behaviour include confinement within a stable,
240 reduced opportunity for social contact or an anticipatory/frustration element [24 &
241 25]. One study found that the type and quantity of forage provided, bedding, yard
242 size and tactile contact with neighbouring horses while stabled influenced the
243 occurrence of weaving [21]. It may be that horses that weaved in our cohort had
244 differing aspects of their general management compared to those that did not weave

245 or that aspects of their management may be linked to both weaving and colic risk,
246 although this an area requiring further investigation.

247

248 Increasing time spent at pasture was found to be associated with a decreased risk of
249 recurrent colic in the present study. This is in agreement with three previous studies
250 investigating the risk of colic [11, 17 & 26] and may reflect the beneficial effects of
251 grazing perhaps in combination with the ability to exercise and opportunities to
252 interact with the natural environment. The equine gastrointestinal tract has evolved
253 to be optimally adapted for trickle feeding and a forage based diet. Providing suitable
254 access to pasture may go some way to meet these physiological requirements
255 however additional attention may be required to ensure pasture is appropriately
256 managed in order to balance out the management of colic risk and other medical
257 conditions. This may include; pasture analysis to examine whether suitable grass
258 types and other plant species are present, limiting parasitic exposure, and
259 maintaining an appropriate stocking density as a few examples. Within this study,
260 ‘access to pasture’ included only those horses that were turned out onto grass
261 paddocks/fields and we found no association with acreage or stocking density and
262 the risk of recurrence. Any change in the amount of time spent at pasture is likely to
263 constitute a change in diet, itself a risk factor for colic. For this reason it is advisable
264 that any changes are introduced slowly.

265 Feeding fruit and vegetables was found to be associated with a decreased risk of
266 colic within this cohort although this finding should be interpreted with caution and
267 may not be applicable to other populations. The exposure was recorded as a binary
268 variable (feed fruit/veg yes/no) and it was not possible to assess the effect of
269 frequency, type or quantity fed due to small numbers within the sample. Therefore it
270 is not possible to make recommendations on how to incorporate fruit and vegetables
271 into the diet to alter colic risk. One possibility is this may be a proxy measure for
272 dietary practices of particular types of owners or other management factors not
273 accounted for within these data. This finding requires additional research in order to
274 understand the impact of feeding fruit and vegetables on colic risk in practice. One
275 study investigating feeding preferences in horses found that some fruit and vegetable
276 flavours increased the acceptance and rate of consumption of food [27]. If such
277 feeding behaviour is interpreted by owners as the horse enjoying the food then this

278 may motivate some owners to provide such foods within the diet. Further work is
279 warranted to examine dietary decisions made by different types of horse-owners and
280 to understand the motivations behind feeding behaviours and their potential impact
281 on equine health.

282 A significant interaction was found whereby the increased risk associated with
283 CBWS was modified by additionally feeding fruit and vegetables. It may be for
284 example that feeding fruit and vegetables is associated with particular management
285 factors such as catching horses in the field, and the availability of turn out could
286 potentially link this finding with CBWS although it is unclear from this data how to
287 interpret this effect. This finding adds credence to the possible protective role of
288 feeding fruit/vegetables reported above; however it is not possible to recommend
289 how to incorporate these into the diet from this data. A Chi-square test indicated that
290 those horses fed fruit/vegetables were no less likely to display CBWS behaviour than
291 those not fed fruit/vegetables. Another study found a significant interaction between
292 crib-biting and carer of the horse and proposed that this may be due to the way in
293 which particular types of carers approach the management of horses [16]. It may be
294 that carers differ in their motivations and decision making for the types of food
295 offered to their horses and this may be influenced by their attitudes surrounding the
296 needs of horses with CBWS behaviour.

297 The finding that probiotics may be associated with an increased risk of recurrent
298 colic should be interpreted with caution. The confidence intervals cross one and this
299 variable was not statistically significant ($p=0.055$) but its inclusion improved the
300 overall fit of the model. It is possible that administering probiotics is a marker for
301 certain types of horses that already have an inherent risk of colic e.g. older horses,
302 those with dental problems, those prone to laminitis or with previous episodes of
303 colic. There is little evidence on the effect of feeding probiotics on equine colic.
304 Although not directly comparable to this study of an adult equine population (where
305 a variety of different probiotics were used), one study reported the administration of
306 *Lactobacillus pentosus* WE7 preparation to be associated with diarrhoea and signs of
307 colic in foals [28]. Another study reported a beneficial effect with feeding probiotics
308 to horses with acute enterocolitis leading to a reduction in hospitalisation time [29].
309 Nevertheless, questions remain about the efficacy of probiotic preparations and
310 further clinical trials are required to investigate their therapeutic potential in horses

311 especially as many preparations are available via the veterinary market [30] and
312 appear popular among some owners.

313 One of the study limitations was that it was not possible to identify the cause of colic
314 in most cases. This is commonly the case among medical colic treated in general
315 practice with one study reporting 72% of colic cases seen over 2 years were
316 spasmodic/undiagnosed colic [3]. The underlying cause of such undiagnosed colic
317 may be multifactorial with a range of presentations [31]. It is possible that
318 misclassification bias may have been introduced where owner reported colic cases
319 were included in the analysis. However, all further episodes of colic (or suspected
320 colic for the owner reported episodes) were assessed according to whether the
321 described episode fitted the case criteria for colic (as outlined within the methods). It
322 was considered that the combination of the fulfilment of the case criteria, assessment
323 of the reported signs of colic (see [6] for further details) along with the owners'
324 experience of a veterinary diagnosed medical colic would improve the assumption
325 that these owner reported colic episodes were correctly reported in order to reduce
326 this potential bias. Within this study we did not find an association with exercise
327 (type or frequency) and the risk of recurrence. Additionally, we did not collect blood
328 or faecal samples from this cohort for parasitological investigations. Previous studies
329 have suggested a link between gastrointestinal parasites (e.g. tapeworm associated
330 colic [32] or more rarely, thromboembolic disease / verminous arteritis caused by
331 *Strongylus vulgaris* [31] associated with recurrent colic). We measured factors that
332 may be considered proxy measures for parasitic exposure such as use of anthelmintic
333 products (frequencies and types); pasture management approaches, stocking density,
334 co-grazing and some exploration of how owners decide upon approaches to parasite
335 control. However, none of these factors were influential in the final model.

336 ***Conclusions and practical relevance***

337 Horses that have experienced a colic episode are known to be at increased risk of
338 future episodes. In this study we report risk factors that provide further evidence to
339 support managerial approaches to colic prevention namely the provision of access
340 to grazing. The behavioural risk factors identified (CBWS and weaving) highlight
341 individual horses that may be at higher risk for recurrent colic and therefore it would
342 seem appropriate that particular attention is paid to their colic prevention strategies

(e.g. diet, access to grazing, anthelmintic prophylaxis and dental care). Further studies to investigate the mechanisms by which these behaviours influence the risk of colic are warranted.

Table 1: Multivariable logistic regression model of risk factors associated with recurrence of colic in the general horse population in North West England

	Category	Odds ratio	Lower 95% confidence interval	Upper 95% confidence interval	Likelihood ratio p-value
Crib-biting or windsucking (CBWS) behaviour	No (Ref)	1.0			
	Yes	10.1	2.5	41.0	<0.001
Weaving behaviour	No (Ref)	1.0			
	Yes	3.9	1.5	10.1	0.004
Time spent at pasture (hours per day / week)		0.99	0.99	1	0.005
Fruit / vegetables in diet	No (Ref)	1.0			
	Yes	0.5	0.2	1.3	0.16
Probiotics in diet	No (Ref)	1.0			
	Yes	2.4	0.99	6.0	0.06
Interaction term: Windsucking x fruit/vegetables in diet		0.03	0.002	0.5	0.005

Based on 56 cases and 159 controls. Hosmer-Lemeshow test statistic p=0.446.

Ref=Reference category

Explanation of interaction term

- No fruit/vegetables and horse does not display CBWS behaviour, OR = 1
- No fruit/vegetables and horse displays CBWS behaviour, OR = 10.1
- Yes fruit/vegetables and horse does not display CBWS behaviour, OR = 0.5
- Yes fruit/vegetables and horse displays CBWS behaviour, OR= (10.1 x 0.5 x 0.03) = 0.15

Table 2: Decreasing risk of recurrent colic with time spent at pasture

Time spent at pasture	Number of hours per week	Odds ratio of risk of recurrent colic
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1 hour / day / week	7	0.93
3 hrs / day / week	21	0.81
6 hrs / day / week	42	0.66
12 hours / day / week	84	0.43
24 hours / day / week	168	0.18

359

360 **References**

361 [1] Mellor, D.J., Love, S., Walker, R., Gettinby, G. and Reid, S.W.J. (2001) Sentinel
362 practice-based survey of the management and health of horses in Northern Britain. Vet. Rec.
363 **149**, 417-423.

364

365 [2] Mair, T. S. (2004) BEVA evidence-based medicine colic survey. In: Proceedings British
366 Equine Veterinary Association Congress Birmingham, UK 58-59.

367

368 [3] Proudman, C. J. (1991). A 2-year prospective survey of equine colic in general practice.
369 Equine vet. J. **24**(2), 90-93.

370

371 [4] Hart, S. and Southwood, L.L. (2010) The enigma of post operative recurrent colic:
372 Challenges with diagnosis and management. Equine vet. J. **22** (8), 408-411.

373

374 [5] Beard, W.L. and Freeman, D.E. (1994) Clinical case conference. J. Am. vet. med. Ass.
375 **204**, 1165.

376

377 [6] Detail to be provided upon acceptance.

378 [7] Archer, D. C. and Proudman, C.J. (2006) Epidemiological clues to preventing colic. The
379 Vet. J. **172**(1), 29-39.

380 [8] Tinker, M.K, White, N.A., Lessard, P., Thatcher, C.D., Pelzer, K.D., Davis, B. and
381 Carmel, K. (1997) Prospective study of equine colic risk factors. Equine vet. J. **29** (6), 454-
382 458.

383

384 [9] Cohen, N.D., Gibbs, P.G. and Woods, A.M. (1999) Dietary and other management
385 factors associated with colic in horses. J. Am. vet. med. Ass. **215** (1), 53-60.

386

387 [10] Cohen, N. D., P. L. Matejka, Honnas, C.M. and Hooper, N.R. (1995) Case-control
388 study of the association between various management factors and development of colic in
389 horses. J. Am. vet. med. Ass. **206**(5), 667-673.

390
391 [11] Hillyer, M. H., Taylor, F. G. R., Proudman, C. J., Edwards, G. B., Smith, J. E., and
392 French, N. P. (2002) Case control study to identify risk factors for simple colonic
393 obstruction and distension colic in horses. Equine vet. J. **34** (5), 455-463.

394
395 [12] Cohen, N. D. and Peloso, J.G. (1996) Risk factors for history of previous colic and for
396 chronic, intermittent colic in a population of horses J. Am. vet. med. Ass. **208**(5), 697-703.

397
398 [13] Archer, D. C., Proudman, C.J., Pinchbeck, G., Smith, J.E., French, N.P. and Edwards,
399 G.B. (2004) Entrapment of the small intestine in the epiploic foramen in horses: a
400 retrospective analysis of 71 cases recorded between 1991 and 2001. Vet. Rec. **155**(25), 793-
401 7.

402
403 [14] Reeves, M. J., Salman, M. D. and Smith, G. (1996) Risk factors for equine acute
404 abdominal disease (colic): Results from a multi-center case-control study. Prev. vet. Med.
405 **26**(3-4), 285-301.

406
407 [15] Nadeau, J.A. and Andrews, F.M. (2009) Equine gastric ulcer syndrome: The continuing
408 conundrum. Equine vet. J. **41** (7), 611-615.

409
410 [16] Archer D.C., Pinchbeck, G.L., French, N.P. and Proudman, C.J. (2008) Risk factors for
411 epiploic foramen entrapment colic: an international study. Equine vet. J. **40** (3), 224-230.

412
413 [17] Archer, D.C., Pinchbeck, G.L., French, N.P. and Proudman, C.J. (2008) Risk factors for
414 epiploic foramen entrapment colic in a UK horse population: A prospective case-control
415 study. Equine. Vet. J. **40** (4), 405-410.

416
417 [18] Hatsie, T. and Tibshirani, R. (1986) Generalized Additive Models. Statistical Sciences **1**
418 (3), 297-310.

419 [19] Dahoo, I., Martin, W. and Stryhn, H. (2003) Veterinary Epidemiologic Research AVC
420 Inc. University of Prince Edward Island p 360.

421

- 422 [20] Malamed, R., Beger, J., Bain, M.J., Kass, P. and Spier, S.J. (2010) Retrospective
423 evaluation of crib-biting and windsucking behaviours and owner-perceived behavioural
424 traits as risk factors for colic in horses. *Equine vet. J.* **42** (8), 686-692.
- 425 [21] McGreevy, P.D., Cripps, P.J., French, N.P., Green, L.E. and Nicol, C.J. (1995)
426 Management factors associated with stereotypic and redirected behaviour in the
427 Thoroughbred horse. *Equine vet. J.* **27** (2), 86-91.
- 428 [22] Redbo, I., Redbo – Torstensson, P., Oldberg, F.O., Hedendahl, A. and Holme, J. (1998)
429 Factors affecting behavioural disturbances in race-horses. *Anim. Sci.* **66**, 475-481.
- 430 [23] Escalona, E., Merrifield, C., Proudman, C., Holmes, E. (2012) Metabolomics of
431 Thoroughbred racehorses: a pilot study. Abstract at 9th Annual International
432 Conference of the Metabolomics Society.
- 433 [24] Nicol, C. (1999) Understanding equine stereotypies. *Equine vet. J.* **28**, 20-25.
- 434 [25] Mills, D.S. and Nankervis, K.J. (1999) *Equine behaviour: Principles and practice*
435 Published by: Blackwell Science.
- 436 [26] Hudson, J.M., Cohen, N.D., Gibbs, P.G. and Thompson, J.A. (2001) Feeding practices
437 associated with colic in horses. *J. Am. vet. med. Ass.* **219** (10), 1419-1425.
- 438 [27] Goodwin, D., Davidson, H.P.B. and Harris, P. (2005) Selection and acceptance of
439 flavours in concentrate diets for stabled horses. *Appl. Anim. Behav. Sci.* **95** (3-4), 223-232.
- 440 [28] Weese, J.S. and Rousseau, J. (2005) Evaluation of *Lactobacillus pentosus* WE7 for
441 prevention of diarrhoea in neonatal foals. *J. Am. Vet. Med. Ass.* **226** (12), 2031-2034.
- 442 [29] Desrochers, A.M., Dolente, B.A., Roy, M.F., Boston, R. & Carlisle, S. (2005) Efficacy
443 of *Saccharomyces boulardii* for treatment of horses with acute enterocolitis. *J. Am. Vet.*
444 *Med. Ass.* **227**, 954-9.
- 445 [30] Weese, J.S. and Martin, H. (2011) Assessment of commercial probiotic bacterial
446 contents and label accuracy. *Can. Vet. J.* **52**, 43-46.
- 447
- 448
- 449
- 450
- 451
- 452
- 453
- 454
- 455
- 456
- 457

458 [31] Hillyer, M. H. and Mair, T. S. (1997) Recurrent colic in the mature horse: a
459 retrospective review of 58 cases. Equine vet. J. **29** (6), 421-4.
460
461 [32] Proudman, C.J. & Holdstock, N.B. (2000) Investigation of an outbreak of tapeworm-
462 associated colic in a training yard. Equine Vet. J. supp **32**, 37-41.
463
464 Supplementary material
465 Table 1: Univariable results of risk factors associated with recurrence of colic ($p < 0.2$).
466 Table 2: Univariable results of factors found to have no significant association with
467 recurrence of colic ($p\text{-value} > 0.2$)
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