# 1 Cohort study of the success of controlled weight loss programs for

## 2 obese dogs

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42 Abstract

43

44 Background: Most weight loss studies in obese dogs assess rate and percentage of weight loss in the first 2-3 months, rather than the likelihood of successfully reaching target weight. 45 46 47 **Objective:** To determine outcome of controlled weight loss programs for obese dogs, and to 48 determine the factors associated with successful completion. 49 50 Animals: 143 obese dogs undergoing a controlled weight loss program. 51 52 Methods: This was a cohort study of obese dogs attending a referral weight management 53 clinic. Dogs were studied during their period of weight loss, and cases classified according to outcome as "completed" (reached target weight), "euthanized" (was euthanized before 54 55 reaching target weight), or "stopped prematurely" (program stopped early for other reasons). 56 Factors associated with successful completion were assessed using simple and multiple 57 logistic regression. 58 59 Results: 87/143 dogs (61%) completed their weight loss program, 11 [8%] died or were euthanized, and the remaining 45 [32%] stopped prematurely. Reasons for dogs stopping 60 61 prematurely included inability to contact owner, refusal to comply with weight management

advice, or development of another illness. Successful weight loss was positively associated with a faster rate (P<0.001), a longer duration (P<0.001), and feeding a dried weight management diet (P=0.010), but negatively associated with starting body fat (P<0.001), and use of dirlotapide (P=0.0046).

67 Conclusions and Clinical Relevance: Just over half of all obese dogs on a controlled weight 68 loss program reach their target weight. Future studies should better clarify reasons for 69 success in individual cases, and also the role of factors such as activity and behavioral 70 modification.

## 72 ABBREVIATIONS

73	AAFCO	Association of American Feed Control Officials
74	AF	as fed
75	BMD	Bernese mountain dog
76	CKCS	Cavalier King Charles spaniel
77	CI	confidence intervals
78	DEXA	dual-energy X-ray absorptiometry
79	DM	dry matter
80	EBT	English bull terrier
81	F	female
82	FCR	Flat coated retriever
83	FOS	fructo-oligo saccharides
84	GR	Golden retriever
85	GSD	German shepherd dog
86	HPHF	high protein high fiber
87	HPMF	high protein medium fiber
88	М	male
89	ME	metabolizable energy
90	MER	maintenance energy requirement
91	NF	neutered female
92	NM	neutered male
93	OR	odds ratio
94	SBT	Staffordshire bull terrier
95	STROBE	Strengthening and reporting of observational studies in epidemiology
96	TDF	total dietary fiber

97 YT Yorkshire terrier

## 99 Background

100

101	The medical profession classifies human obesity as a disease, <sup>1</sup> and it is arguably the most
102	important medical disease in dogs. <sup>2</sup> Recent studies have suggested that approximately half of
103	all pet dogs are overweight <sup>3,4</sup> and that the prevalence has been steadily increasing. <sup>5</sup> Obesity is
104	associated with many diseases, including orthopedic disease, diabetes mellitus, respiratory
105	disease, and certain types of neoplasia. <sup>2,3</sup> Dogs that are overweight might also develop
106	metabolic derangements, <sup>6,7</sup> altered renal function, <sup>8</sup> and respiratory dysfunction causing poorer
107	oxygenation. <sup>9</sup> Obese dogs have a reduced quality of life, <sup>10</sup> and a shorter lifespan. <sup>11</sup> Given the
108	large at-risk population, and the effects on health and quality of life, obesity is a major
109	welfare concern. Management usually involves controlled weight loss through energy
110	restriction using a purpose-formulated weight loss diet coupled with increased activity, <sup>12-15</sup>
111	but licensed drug therapies are also available. <sup>16,17</sup>

112

113 The benefits of controlled weight loss in obese dogs are well established, with evidence of improvement in disease status,<sup>18</sup> reversal of metabolic derangements,<sup>6,7</sup> and improved quality 114 of life.<sup>10</sup> However, studies are often of short duration, only assessing the initial phase of 115 116 weight loss (e.g. first 2-3 months), and often use colony dogs with experimentally-induced obesity rather than client owned-dogs with naturally occurring disease.<sup>16-18</sup> As a result, 117 118 simple outcomes are studied such as rate of weight loss, percentage weight loss and energy intake required to achieve weight loss.<sup>13,14</sup> Arguably, studies that assess the whole of the 119 120 weight loss period and beyond are more desirable, and also focus outcomes such as success of reaching and maintaining target weight.<sup>19</sup> Human studies suggest that weight loss usually 121 122 plateaus at 6 months on diet-based weight loss program, with most people never reaching their target weight,<sup>20</sup> or subsequently regaining a substantial amount within one year.<sup>21</sup> To the 123

authors' knowledge, only one previous study of dogs has reported success of a weight loss
program,<sup>15</sup> although the weight loss period was short (6 months), and it was not clear whether
all dogs had reached their target weight. In light of the limited information, the aims of the
current study were, first, to determine the proportion of obese dogs commencing a diet-based
weight loss program that successfully reached target weight and, second, to identify factors
associated with success.

131 Methods

#### 132 Study design

This was a cohort study of obese client-owned dogs designed to determine the outcome of
controlled weight loss programs and the factors associated with successful completion. It has
been reported according to the Strengthening and Reporting of Observational Studies in
Epidemiology (STROBE) statement guidelines.<sup>22</sup>

137

#### 138 Animals

139 The dogs in the cohort studied were all referred to the Royal Canin Weight Management 140 Clinic, University of Liverpool UK, for investigation and management of obesity. Eligible 141 cases were: originally seen between November 2004 and July 2012, started a weight 142 management program, and reached a known end-point for their weight loss (i.e. completed, 143 stopped prematurely, or died [see below]) by February 2013. Additional eligibility criteria 144 included having data available from the preliminary investigations undertaken prior to weight 145 loss (see below), and having had body composition analysis conducted by dual-energy X-ray absorptiometry (DEXA).<sup>23</sup> Given the study timeframe and broad eligibility criteria, dogs used 146 147 in previous studies assessing weight loss in selected cases that successfully lost weight only,<sup>13,14</sup> and also in a study examining subsequent rebound after successful weight loss.<sup>19</sup> 148 149 However, none of these studies examined the proportion of cases starting a weight loss 150 program that successfully reached target weight. The study protocol adhered to the 151 University of Liverpool Animal Ethics Guidelines, and was approved by the University of 152 Liverpool Research Ethics committee, the Royal Canin ethical review committee, and the 153 WALTHAM ethical review committee. Owners of all participating animals gave informed 154 consent in writing.

#### 156 Weight loss regimen

Complete details regarding the weight loss protocol used at the clinic have been described.<sup>13,14</sup> 157 158 Briefly, dogs were determined to be systemically well, and without abnormalities that would 159 make controlled weight loss inappropriate by complete blood count, serum biochemical 160 analysis and urinalysis. Serum free thyroxine concentration was measured by equilibrium 161 dialysis at an accredited external laboratory<sup>a</sup> to determine thyroid status. Throughout weight loss, dogs were weighed on electronic scales,<sup>b</sup> which were regularly calibrated using certified 162 163 test weights.<sup>c</sup> Body composition was analyzed before and after the weight loss regime in all dogs, using fan-beam DEXA.<sup>d</sup> Body composition results from before weight loss were used 164 to estimate ideal weight.<sup>10,19</sup> Briefly, the body composition data were entered into a computer 165 166 spreadsheet,<sup>e</sup> containing a purpose-created mathematical formula to predict expected body 167 composition after weight loss at different weights. The predictive equation was based upon typical body composition results from previous weight clinic studies.<sup>13,14</sup> This enabled an 168 169 appropriate ideal body weight to be set, for the individual dog, to be used in energy intake 170 calculations.

171

172 One of three purpose-formulated weight management diets was used for the weight loss protocol (Table 1), namely a high protein high fiber dry diet (HPHF dry),<sup>f</sup> a high protein 173 174 medium fiber dry diet (HPMF dry),<sup>g</sup> and a high protein medium fiber wet diet (HPMF wet),<sup>h</sup> 175 The choice of whether to feed dry food, wet food or a mix of the two depended upon what the 176 owner had fed the dog prior to the weight loss period. Owner and dog preference was also 177 used when choosing between the HPMF and HPHF dry diets (e.g. whether high fiber diets 178 had been tolerated in the past). However, diet choice also depended upon availability and 179 whether any reformulations had occurred. In this respect, both HPMF diets (dry and wet) 180 were available for the whole of the study period, and the formulation did not change.

However, the HPHF diet first became available in June 2006, and was then reformulated in
2010 with a slight increase in moisture content, without major changes in the nutrient profile
(Table 1), with 22 dogs of the 88 dogs fed this diet receiving the reformulated version. The
ME content of both formulations was marginally different (before reformulation: 2900
Kcal/kg; after reformulation: 2865 Kcal/kg).

186

187 The initial food allocation for weight loss was determined by first estimating maintenance energy requirement (MER=440kJ [105Kcal]  $\times$  body weight [kg]<sup>0.75</sup>/day)<sup>24</sup> using the ideal 188 189 weight of the dog, as determined by DEXA. The degree of restriction for each dog was then 190 individualized based upon gender and other factors (i.e. presence of associated diseases), and was typically between 50-60% of MER at target weight.<sup>13</sup> Owners also received tailored 191 advice on lifestyle and activity alterations to assist in weight loss. Further, five dogs whose 192 193 weight loss had been slow also received oral dirlotapide<sup>1</sup> to aid weight loss, whilst four 194 additional dogs had concurrent hypothyroidism (two diagnosed at the referring veterinarian, 195 and two diagnosed at the time of initial referral) and also received levothyroxine. 196

197 Dogs were reweighed every 7-28 days and changes made to the weight loss plan if necessary.<sup>13,14</sup> Throughout the weight loss period, owners maintained a diary in which they 198 199 recorded feeding of the purpose-formulated diet (amount offered and consumed), and any 200 additional food that had been consumed (either given as treats or stolen). At each re-201 evaluation, progress was assessed and changes were made to the weight loss plan, as 202 necessary. Where progress was good (e.g. weight loss of 0.5-2.0% per week in the first 6 203 months, and >0.3%/week thereafter), the weight loss protocol was not adjusted, except that 204 the owner was always encouraged to increase activity whenever possible. If weight loss was 205 deemed to have stalled (defined as either no change [0%] in weight or a gain of weight

206 between two appointments that were at least 14 days apart) or was deemed to be slow 207 (<0.5%) week in the first 6 months, and <0.3% week thereafter), the potential causes were 208 investigated based upon the information provided by the owner in diary records and 209 discussions during the consultation. If poor compliance to the weight loss protocol was 210 thought to be the cause, (i.e. additional food had been consumed) the amount of food fed was 211 not altered, and advice was given to restore compliance; if the dog's activity levels had been 212 less, then advice regarding activity was reiterated; however, where no obvious reason for poor 213 progress could be identified, the amount of food fed was reduced by a readily-calculated 214 amount (e.g. 5g dry food for small dog or 10g for large dog; <sup>1</sup>/<sub>4</sub> sachet of wet food for a small 215 dog or  $\frac{1}{4}$  x 400g can for large dog) on each occasion. When weight loss was deemed to be 216 too quick (>2%/week) the amount of diet was increased in similar increments. In addition to 217 the official reweighs, contact was maintained at other times either by phone or email.

218

### 219 Classification of final outcome

220 Dogs were assigned to three groups, according to their outcome, as follows. Dogs that lost 221 weight and reached their target were classified as 'completed'. Dogs that were euthanized 222 before reaching target weight were classified as 'euthanized', and the reason was recorded 223 where it was known. Finally, dogs that did not complete for other reasons were classified as 224 'stopped prematurely', and again the reason was recorded where it was known. This latter 225 category included all dogs lost to follow up because their owners stopped attending the clinic. 226 In such cases, owners were contacted at least 3 times by their preferred method of contact 227 (telephone or email), and at least once by post.

228

### 229 Statistical Analysis

230 All data are expressed as median (range), except where indicated, and there were no missing data. Statistical analyses were performed with computer software,<sup>j</sup> with the level of 231 232 significance set at P < 0.05 for two-sided analyses. Given that this was an observational cohort 233 study, and no such study had previously been conducted, a sample size calculation was not 234 performed. Instead, the principle determinant of sample size was the number of dogs seen 235 that met the eligibility criteria during the study timeframe. The Shapiro-Wilk test was used to 236 determine whether or not datasets were normally distributed, and either parametric or non-237 parametric tests were then performed as appropriate. For continuous variables, differences 238 amongst groups were assessed with the Kruskal-Wallis test, with post hoc comparisons made, 239 where appropriate, using the Dwass-Steel-Critchlow-Fligner test.

240

241 The continuous variables analyzed by groups were age, body fat percentage before weight 242 loss, percentage weight loss, duration of weight loss, rate of weight loss, metabolizable 243 energy intake during weight loss, the number of times weight loss stalled (i.e. when there was 244 no change in weight or weight gain between appointments), and the number of diet energy 245 intake changes (i.e. when the weight management clinic staff adjusted down the daily food 246 intake at the time of a recheck). Overall percentage weight loss and rate of weight loss were 247 both expressed as a proportion of starting weight lost, and reported rates of weight loss are the 248 average of the whole weight loss period. Duration of weight loss was calculated from the 249 date of the first appointment to the date when target weight was reached (for those 250 completing), or to the last available weight record (for those not completing). Where dogs 251 were enrolled but then did not return for any reassessments, the duration was recorded as 0 252 days.

253

254 Categorical variables were compared, amongst dogs with different outcomes, using Fisher's 255 exact test, and those assessed included breed, sex, neuter status, diet characteristics, 256 concurrent hypothyroidism, and use of dirlotapide. The effect of breed was determined by 257 first creating dummy variables for all breeds with more than 5 individuals (where  $1 = \log of$ 258 that breed;  $0 = \log \operatorname{not} \operatorname{of} \operatorname{that} \operatorname{breed}$ ). For sex comparisons, a dummy variable was created 259 whereby male dogs were scored as 1 and female dogs as 0; a dummy variable was also 260 created for neuter status whereby neutered dogs were scored as 1 and intact dogs as 0. The 261 effect of diet was assessed in two ways: first, a dummy variable was created whereby 262 comparing dogs fed dry food exclusively (including both those on HPHF and HPMF diets) 263 were assigned a score of 1, to those fed either wet food exclusively, or a combination of dry 264 and wet food were assigned a score of 2; second, where dogs were fed dry food exclusively, 265 the type of dry food was also compared (1=HPHF diet; 0=HPMF).

266

267 In order to take account of possible confounding factors on the results obtained, logistic regression was performed. The outcome variable tested was success with weight loss, 268 269 whereby dogs completing weight loss were assigned a score of 1, and those not completing 270 were assigned a score of 0. Both 'intention-to-treat' (whereby dogs that were euthanized were 271 included in the group not completing), and 'per-protocol' (whereby dogs that were euthanized 272 were excluded) analyses were conducted. Initially, all variables listed above were tested 273 separately with simple logistic regression. A multiple logistic model was then built, which 274 initially included the variables identified as P < 0.2 in simple regression. The model was then 275 refined over multiple rounds using backwards-stepwise elimination, of the least significant 276 variable each time, and variables were only retained in the final model if they were significant 277 (P < 0.05). Logistic regression results are reported as odds ratios (OR), 95% confidence 278 intervals (95% CI) and the associated *P*-value.

#### 280 **Results**

283

#### 281 Study animals and outcomes of weight loss

282 During the period of study, 160 dogs were referred to the clinic. Of these, 143 met the

eligibility criterion of having a defined endpoint, and there were no missing data for any

variable. The other 17 dogs were excluded because the weight loss period had not been

completed at the time of data review. Of the 143 dogs, 87 (61%) completed, 11 (8%) were

euthanized (by the referring veterinarian), and 45 (31%) stopped prematurely. Full details of

all dogs finally included are given in Table 2. There were no differences in the proportions of

288 the five most frequent breeds amongst groups (P>0.05 for all), and no differences for sex

289 (P=0.57), starting weight (P=0.75) and body fat mass (P=0.16). However, age was different

amongst groups (P=0.045), with dogs that were euthanized being older than those that

completed the weight loss protocol. Three of the hypothyroid dogs completed the weight loss

292 protocol, with the other dog stopping prematurely.

293

## 294 **Outcomes of weight loss**

Details of the outcomes of weight loss are reported in Table 3. For the whole cohort,
percentage weight loss was 19.5 % (range -3.0 % to 43.9 %), median duration was 200 days

297 (range 0-1149 days), and the corresponding rate of weight loss was 0.6 % per week (-0.3 to

298 2.2 % per week).

299

#### 300 Comparison of baseline variables amongst groups

301 Comparisons were made amongst the three outcome groups (e.g. completed, euthanized, and

302 stopped prematurely) for all baseline variables (Table 2). There were no differences in the

303 proportions of the five most frequent breeds amongst groups (*P*>0.05 for all), and no

differences for sex (P=0.57), starting weight (P=0.75) and body fat mass (P=0.16). However,

305 age was different amongst groups (P=0.045), with dogs that were euthanized being older than 306 those that completed the weight program.

307

## 308 Comparison of weight loss outcomes amongst groups

309 Comparisons were made amongst the three outcome groups (e.g. completed, euthanized, and 310 stopped prematurely) for all weight loss (Table 3). There were no differences in the median 311 daily energy intake (per kg metabolic body weight) amongst groups (P=0.67), and also no 312 differences for the number of times weight loss process stalled (P=0.37), the number of times 313 food intake had to be reduced (P=0.16), and the use of dirlotapide (P=0.082). However, dogs 314 that succeeded remained on their weight loss program longer (P < 0.001), had faster overall 315 rates of weight loss (P=0.001), and lost more weight overall (P<0.001). An effect of diet type 316 was also seen, with more of the completing dogs having been fed dry food than either wet 317 food or a mix of types (P=0.0077). However, there were no group differences in the type of 318 dry food used (i.e. HPHF vs. HPMF diets, P=0.54).

319

#### 320 Logistic regression analysis to determine factors associated with success

321 Given that a number of group differences were evident, logistic regression analysis was then 322 used to determine factors associated with success, when taking account of any possible 323 confounding. When assessed on an intention-to-treat basis, simple logistic regression (Table 324 4) identified that rate of weight loss (P=0.0092), duration of weight loss (P=0.014) and diet 325 type (P=0.028) were positively associated with success, whilst starting body fat was 326 negatively associated with success (P=0.029). Other factors were not significantly associated 327 with weight loss, but qualified (at P < 0.2) for inclusion in the initial multiple regression model 328 including: age, breed (with Mixed Breed, Golden Retriever, and Yorkshire Terrier included 329 independently), dirlotapide use, number of weight loss stalls, and number of changes to the

330 weight loss plan (Table 4). After the initial model was refined by backwards stepwise 331 elimination, the best-fit model was one that included six factors. Factors positively associated 332 with success included being of mixed breed (P=0.039), being fed a dry weight loss diet 333 (P=0.0095), rate of weight loss (a faster rate of weight loss in completing dogs, P<0.001), and 334 duration (a longer duration or weight loss in completing dogs, P<0.001), whilst factors 335 negatively associated with success included starting percentage body fat (P < 0.001), and 336 dirlotapide use (P=0.0046). When data were instead analyzed on a per protocol basis by 337 excluding dogs that were euthanized, results were similar, except that the breed effect was no 338 longer evident (Table 4). Given that dogs fed wet food or a mix of food types were less 339 successful, there was a concern such a categorization might have inadvertently selected for 340 dogs with problematic feeding habits, since this category included those where diet type had 341 been changed. As a result, the analyses were repeated only to include dogs that had remained 342 on the same diet type for the whole of weight loss. Once again, a diet effect remained (simple 343 regression: OR 10.41, 95%-CI 1.22-89.00, P=0.032; multiple regression: OR 32.50, 95%-CI 344 2.02-458.68, *P*=0.016).

## 345 **Discussion**

346 This large study assesses the success of obese dogs at completing a controlled weight loss 347 program and at reaching target body weight. The finding that 40% of dogs stopped prematurely is similar to a previously published study,<sup>15</sup> and suggests that controlled weight 348 349 loss is challenging. However, whilst somewhat disappointing, this response rate is better than 350 for humans who use diet-based strategies for losing weight where few individuals succeed with weight loss.<sup>20</sup> The weight loss period is only one aspect of the overall weight 351 352 management process, which also includes maintaining weight long term and avoiding 353 rebound. The fact that this aspect was not assessed in the current study is a limitation, 354 although the population studied did include cases that also participated in a previous study 355 that did specifically assess maintenance of weight in the post-weight-loss period.<sup>19</sup>

356

357 The large cohort size meant that we could also determine factors associated with success: 358 associations were found with starting body fat percentage, overall rate of weight loss, duration 359 of weight loss, and the type of food used. Given that the study was observational in nature, 360 the reasons for such associations are not always clear and causality cannot necessarily be 361 assumed, i.e. that the factors identify cause the dogs to complete or stop prematurely. Direct 362 associations are more likely when associations are identified with factors present at the outset 363 of the controlled weight loss program, such as body fat mass. Here, it is reasonable to 364 speculate that the negative association between starting body fat mass and the outcome of 365 weight loss might be causally related, and to suggest that the most overweight dogs might 366 struggle to reach target weight. Indeed, this finding is similar to human studies where weight loss plateaus over time,<sup>20</sup> and is not surprising given the metabolic changes that occur upon 367 caloric restriction.<sup>21</sup> In contrast, where the associations identified were with factors not 368 369 present at the outset, conclusions should be more speculative. For instance, successful weight

loss was positively associated with the duration of the weight loss program, and this is most likely to be because the weight loss process was curtailed in cases that stopped prematurely or were euthanized. Therefore, a long duration is a characteristic of the successful case, rather than the cause of it. Nonetheless, whilst care should rightfully be taken when drawing any conclusions from these associations, these observations are still of interest since they might help to develop hypotheses to test in future studies.

376

377 A faster rate of weight loss was also positively associated with success. At first, this 378 observation seems counterintuitive, since faster rates of weight loss should make the weight 379 loss program shorter yet, as stated above, duration was longer in cases that successfully 380 completed. However, the findings can readily be explained by the fact that these associations 381 with duration and rate of weight loss were independent of one another in the final multiple 382 regression model. The faster weight loss rate could be a characteristic of the cases that 383 successfully lose weight, but a causal relationship might exist. In this respect, those owners 384 whose dogs lost weight more rapidly could be motivated to persist with the program for 385 longer, thus improving the likelihood of successfully reaching target weight. Conversely, 386 slow weight-loss progress could cause owner frustration making them more likely to stop 387 prematurely. Of course, whilst such a hypothesis is intriguing, it does not explain why the 388 dogs that stopped prematurely had a slower rate of weight loss in the first place. Possible 389 causes might include lack of compliance with the weight loss program, difference in activity 390 levels, or might be related to the speed of weight gain and development of obesity. A further 391 limitation of the current study was that physical activity was not objectively assessed. 392 Moreover, while owners were always questioned at the first consultation about the speed and 393 duration of weight gain, most were unable to provide any detailed insight into this (for 394 instance because weight had been infrequently recorded). Further work is required to

determine their respective roles of exercise and speed of weight gain on the success of asubsequent weight loss program.

397

398 The study also identified an association between food type and successful weight loss, with a 399 greater proportion of cases fed dry food completing than those on wet food or a mix of wet a 400 dry food. However, the finding should be interpreted cautiously, in light of the fact that only 401 9 dogs were fed wet food or a mixture. One possible explanation for the effect would be 402 differences in macronutrient content of the various diets. Indeed, previous work has indicated 403 that voluntary food intake is less when dogs are fed diets with increased protein and fiber content.<sup>25</sup> and such diets also promote greater fat loss during the weight loss period.<sup>14</sup> 404 405 However, in the current study, the fact that there was no difference in success for dogs on the 406 HPHF and HPMF foods suggests that differences in fiber content were not responsible. Thus, 407 other reasons are likely to account for the positive association between feeding dry food and 408 completing a controlled weight loss program. An alternative possibility would be the fact that 409 some of the dogs on a mixed feeding combination had switched rations during their program, 410 i.e. from dry to wet (or a mix) and vice versa. Whilst the reason for switching strategies was 411 not recorded, it was often because of problems with progress, so that we might have 412 inadvertently selected for less successful dogs. In light of this, we repeated the multiple 413 regression analysis excluding dogs that had switched food type, and the effect of dry food on 414 weight loss outcome remained. Thus, such a selection bias cannot account for effect of food 415 type. A third possibility might be that feeding dry food affords greater control than wet food; 416 the amount of food can be measured out precisely on weigh scales, small adjustments to the 417 amount fed can easily be made, and the food readily lends itself to methods of feeding that 418 promote environmental enrichment, such as the use of puzzle feeders. Such feeders have been shown to slow food intake in dogs,<sup>k</sup> thereby improving satiety with the resulting effect 419

of decreased food-seeking behavior. Finally, owner factors might also explain this
association, whereby the ease of using dry food might have increased compliance, thereby
indirectly improving outcome. The added cost of wet food might have been an additional
disincentive for owners using this format to continue with the weight loss program. Given the
multiple possibilities, further studies are now required both to confirm and to determine
reason for the association between diet type and successful weight loss.

426

427 Another factor that was negatively associated with the completing the weight loss program 428 was use of the microsomal transfer protein inhibitor dirlotapide. Conclusions should be made 429 cautiously because only a small number of dogs received the drug, and it was administered in 430 conjunction with the current weight loss diet, which is not specifically recommended. 431 Although all foods used had 10% fat content (on an as fed basis), and previous studies have 432 suggested a good response to dirlotapide in dogs fed food with an equivalent fat content, dogs were not fed *ad libitum*.<sup>16</sup> This might account for the negative association between 433 434 dirlotapide use and successful weight loss. Alternatively, selection bias could have been 435 responsible, since the drug was used when cases were struggling with a conventional program 436 using dietary caloric restriction. Nonetheless, the finding suggests that drug therapy does not 437 always provide an additional advantage over dietary energy restriction alone in cases 438 struggling to lose weight. Further work is required to understand better the reasons for failure 439 of dirlotapide in the cases in which it was used.

440

Hypothyroidism is associated with obesity in dogs,<sup>3</sup> and 4 cases in the current series were diagnosed with this disease. We chose to include these dogs so as to ensure that our cases were as representative as possible of the obese pet dog population from which they were drawn. Including such cases in the study is a limitation because it introduces a possible

445 confounder, for example if response to a controlled weight loss program differs from that of
446 euthyroid obese dogs. Therefore, we would recommend further work examining the response
447 of hypothyroid dogs to controlled weight loss.

448

449 Breed was associated with outcome of weight loss in the intention-to-treat analysis, with a 450 greater proportion of mixed breed dogs completed compared with pedigree dogs. If genuine, 451 it might either suggest potential genetic influences on the success of weight loss programs, or 452 be related to owner factors (for instance, if the characteristics of a mixed breed dog owner 453 differed from those of a pedigree dog owner). This breed effect was the weakest of all 454 associations identified, and was no longer evident when data were analyzed on a per-protocol 455 basis. Conclusions should be even more cautious because of the limited range of breeds included, as well as the limited numbers of each breed. Therefore, further work is needed to 456 457 confirm this observation before investigating the possible reasons for it further.

458

459 A number of limitations should be considered in addition to those discussed above. First, the 460 use of a cohort design means that the basis for our findings are not clear. Thus, further studies 461 are now needed to confirm these findings and to examine possible mechanisms. Second, the 462 dogs studied were referred to a weight management clinic and, as a result, the findings might 463 not be fully representative of dogs in primary care practice. Third, the use of client-owned, 464 rather than colony, dogs introduced a number of possible confounding variables, both dog and 465 owner related. Dog-specific factors increasing population variability include signalment 466 factors, tendency to scavenge, ability to exercise, and the presence of concurrent disease; 467 owner-specific factors include compliance with the weight management advice on feeding 468 and exercise. In human weight loss studies, non-compliance is common and is a major cause of treatment failure.<sup>26</sup> Whilst the use of client-owned dogs could have affected the reliability 469

of the results, the findings are arguably more representative of the target population, such thatthey are more generalizable than findings from studies in colony dogs.

472

Finally, although numerous factors were considered, the roles lifestyle and activity alterations (including exercise) or behavioral manipulation were not examined. Advice on activity and behavior was given to all clients, which was specific to the circumstances of the owner and the dog. Unfortunately, the nature of the advice made it impossible to assign meaningful categories for analysis. As a result of this limitation, future studies should now be considered to assess the role of both activity and behavioral modifications on the outcomes of controlled weight loss.

480

## 481 **Conclusions**

In summary, the current study demonstrates approximately one half of all obese dogs on a
controlled weight loss program reach their target weight. Associated with success was
starting body fat percentage, with the most obese dogs less likely to reach their target weight.
Since activity and behavioral modification were not specifically assessed in the current study,
future studies should also be considered specifically to examine their role.

488

### 489 **Footnotes**

- 490 <sup>a</sup> Axiom Veterinary Laboratories Ltd, Newton Abbott, Devon, UK
- 491 <sup>b</sup> Soehnle Professional, Backnang, Baden-Württemberg, Germany.
- <sup>c</sup> Blake and Boughton Ltd, Thetford, Norfolk, UK.
- <sup>4</sup>93 <sup>d</sup>Lunar Prodigy Advance; GE Lunar, Madison, Wisc, USA.
- <sup>e</sup> Excel<sup>®</sup>, various versions; Microsoft Corporation. Redmond, WA, USA.
- <sup>f</sup>Canine Veterinary Diet Satiety Dry, Royal Canin, Aimargues, France.
- 496 <sup>g</sup>Canine Veterinary Diet Obesity Management Dry, Royal Canin, Aimargues, France.
- 497 <sup>h</sup>Canine Veterinary Diet Obesity Management Wet, Royal Canin, Aimargues, France.
- <sup>498</sup> <sup>i</sup> Slentrol, Zoetis UK, London, UK.
- 499 <sup>j</sup> Stats Direct version 2.6.8, Stats Direct Ltd.
- <sup>500</sup> <sup>k</sup> German AJ, Towlson E, Holden SL, et al. Long-term follow-up after weight management in
- 501 obese cats. Proceedings of the 55th British Small Animal Veterinary Association Congress,
- 502 Birmingham, UK; April 2012
- 503
- 504

#### 505 **Conflicts of interest**

The following conflicts of interest apply: AJG's Readership is funded by Royal Canin; AJG has also received financial remuneration and gifts for providing educational material, speaking at conferences, and consultancy work; SLH's post at the University of Liverpool is also funded by Royal Canin; the diet used in this study is manufactured by Royal Canin; YQ and VB are employed by Royal Canin; PM is an employee of Mars Petcare.

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580		

#### Table 1. Average composition of diets for weight loss

Criterion	High protein high fiber dry <sup>1</sup> 2900 / 2865 Kcal/kg Per 100g AF g/1000 Kcal (ME)		High protein medium fiber dry3275 Kcal/kg <u>Per 100g AF</u> g/1000 Kcal (ME)		High protein medium fiber wet			
ME content					548 Kcal/kg Per 100g AF g/1000 Kcal (ME)			
Moisture	8 / 10	28 / 33	8	27	86	1569		
Crude protein	30 / 30	103 / 105	34	104	7.0	128		
Crude fat	10 / 10	33 / 33	10	30	2.0	36		
Starch	19 / 18	66 / 61	22	66	2.1	38		
NFE	30 / 29	102 / 100	32	97	2.5	46		
Crude fiber	18 / 16	60 / 58	8	25	1.0	18		
Total dietary fiber	28 / 28	97 / 97	18	56	1.4	26		
Ash	5.3 / 5.7	18 / 20	8.1	25	1.5	27		
Fiber sources	· · · · · ·	eet pulp, FOS, sk, diet cereals	Cellulose, b	Cellulose, beet pulp, diet cereals		Beet pulp, cassia gum, carrageenan		

High protein high fiber (Satiety Support Canine, Royal Canin). High protein medium fiber (Obesity Management Canine, Royal Canin). ME= 

Metabolizable energy content, as measured by animal trials according to the American Association of Feed Control Officials protocol (AAFCO, 

2010); AF= as fed; DM= dry matter; FOS= fructo-oligo-saccharides; NFE= nitrogen-free extract. <sup>1</sup> Diet formulation changed in 2010; figures in column refer to diets used before and after 2010, respectively. 

## **Table 2**. Baseline variables of the study dogs

Variable	Completed (n=87)	Stopped prematurely (n=45)	Euthanized (n=11)	<i>P</i> value <sup>4</sup>	
Breed <sup>1</sup>	Labrador 21 Mixed breed 14 CKCS 9 Golden retriever 7 Yorkshire terrier 7	Labrador 14 Mixed breed 4 CKCS 2 Golden retriever 1 Yorkshire terrier 1	Labrador 0 Mixed breed 1 CKCS 1 Golden retriever 0 Yorkshire terrier 0	Lab: 0.088 Mix: 0.34 CKCS: 0.49 GR: 0.41 YT: 0.41	
	OTHER: Alaskan Malamute, Akita, BMD, Border Collie 3, Cairn Terrier 2, Chihuahua, Cocker Spaniel 2, Corgi, Dachshund, Doberman 2, EBT, FCR, GSD, Irish Setter, JRT, Lhasa Apso, Miniature schnauzer, Pug 4, Samoyed, Schipperke, Shih Tzu	OTHER: Akita, Border Collie, Dachshund 3, Dalmatian 2, English Pointer, GSD, JRT 2, Labradoodle, Lancashire Heeler, Lhasa Apso 2, Patterdale terrier, Poodle, Pug, Rottweiler, Scottish terrier, Springer spaniel 2, Tibetan Terrier	OTHER: Bichon Frise, Boxer English Bulldog, EBT, Lhasa Apso, Newfoundland, SBT, Shih Tzu, Weimaraner		
Reason for stopping or euthanasia		Personal reasons of owner 9, refused help shortly after enrolment 5, repeated failure to comply with program 3, owner chose to stop 7, dog developed another disease (pneumonia) 1, not recorded (could not contact owner) 20	Developed another disease 6 (severe orthopedic disease, metastatic mast cell tumor, splenic neoplasia, laryngeal neoplasia, and concurrent cardiac and renal disease), not recorded 5		
Sex <sup>2</sup>	M 2; NM 47, F 2, NF 36	M 1; NM 25; F 2; NF 17	M 1; NM 5; NF 5	0.76	
Age (Mo)	72 (16-228) <sup>a</sup>	84 (24-156) <sup>ab</sup>	96 (55-144) <sup>b</sup>	0.059	
Start Weight (kg)	32.0 (5.3-77.6)	33.9 (4.4 - 60.8)	27.1 (7.2-100.0)	0.75	

Body fat (%) $^3$	44.8 (27.3-55.0)	46.2 (27.9-60.8)	44.2 (35.3-55.5)	0.10

All data (except diet data) are expressed as median (range). <sup>1</sup> Breed acronyms are as follows: BMD, Bernese mountain dog; CKCS, Cavalier King Charles Spaniel; EBT,
English bull terrier; FCR, Flat Coated Retriever; GSD, German Shepherd Dog; SBT, Staffordshire Bull Terrier. <sup>2</sup> Sex acronyms are as follows: M, male; NM, Neutered male;
F, female; NF, neutered female. <sup>3</sup> Body fat percentage was determined before weight loss using dual-energy X-ray absorptiometry. <sup>4</sup> For breed and sex, *P* values are based
upon Fisher's exact tests (Lab: Labrador, Mix: mixed breed, CKCS: Cavalier King Charles Spaniel; YT: Yorkshire terrier); for age, start weight and body fat, *P* values are
based upon Kruskal Wallis tests. Groups with different letters are significantly different from one another, at *P*<0.05.</li>

#### 596 **Table 3**. Outcomes of weight loss

Variable	Completed (n=87)	Stopped (n=45)	Died (n=11)	<i>P</i> value <sup>4</sup>
Diet (number of dogs) <sup>1</sup>	HPHF dry 58 <sup>a</sup> HPMF dry 27 HPMF wet 0 Mixed 2	HPHF dry 24 <sup>ab</sup> HPMF dry 17 HPMF wet 2 Mixed 2	HPHF dry 6 <sup>b</sup> HPMF dry 2 HPMF wet 2 Mixed 1	<i>HPMF v HPHF: 0.54</i> <i>Dry v Wet/mixed: 0.0077</i>
Weight loss (% start weight)	25.5 (5.5 to 43.9) <sup>a</sup>	8.8 (-3.0 to 33.0) <sup>b</sup>	16.7 (-2.3 to 39.5) <sup>b</sup>	<0.001
Rate of Weight loss (%/week)	0.7 (0.1 to 1.7) <sup>a</sup>	$0.4 (-0.3 \text{ to } 2.2)^{\text{b}}$	0.6 (-0.1 to 1.3) <sup>ab</sup>	0.001
Duration (days)	250 (84 to 796) <sup>a</sup>	139 (0 to 1149) <sup>b</sup>	141 (47 to 371) <sup>b</sup>	<0.001
Energy intake (Kcal/kg <sup>0.75</sup> ideal weight/day)	62.3 (44.0 to 92.9)	63.5 (42.3 to 87.1)	60.8 (51.8 to 75.2)	0.67
Weight loss stalls <sup>3</sup>	1 (0-6)	1 (0-18)	0 (0-6)	0.37
Diet energy intake changes <sup>4</sup>	2 (0-11)	2 (0-13)	2 (0-5)	0.16
Concurrent hypothyroidism	3	1	0	0.78
Dirlotapide	1	4	0	0.082

All data (except diet data) are expressed as median (range). <sup>1</sup> Diet types were as follows: HPHF dry, high protein high fiber dry: HPMF dry, high protein medium fiber dry, HPMF wet, high protein medium fiber wet; Mixed, mixed ration with more than one type (e.g. completed: HPHF dry with HPMF wet [n=2]; stopped prematurely: HPMF dry and wet [n=2]; died: HPHF dry with HPMF wet [n=1]). Energy intake expressed in Kcal of metabolizable energy per kilogram of metabolic body weight of ideal weight (kg<sup>0.75</sup>). <sup>2</sup> For diet, *P* values are based upon Fisher's exact tests; for all other data, *P* values are based upon Kruskal Wallis tests. <sup>3</sup> Number of times the weight loss process stalled. <sup>4</sup> Number of times food intake had to be reduced. Groups with different letters are significantly different from one another, at *P*<0.05.

603	Table 4. Results of the logistic regression analysis determining factors associated with success or failure
604	

• • <i>.</i> •	Intention to treat			Per protocol		
Logistic regression	OR <sup>a</sup>	95% CI <sup>b</sup>	Probability	OR <sup>a</sup>	95% CI <sup>b</sup>	Probability
Simple regression						
Age (per month)	0.99	0.98-1.00	0.13	0.99	0.985-1.005	0.34
Target Body Weight (per kg)	1.00	0.98-1.03	0.78	1.00	0.98-1.03	0.79
Body Fat (per %)	0.94	0.89-0.99	0.029	0.94	0.89-1.00	0.047
Breed						
CKCS <sup>c</sup>	2.04	0.53-7.88	0.30	2.48	0.51-12.00	0.26
Labrador retriever	0.95	0.44-2.08	0.91	0.70	0.32-1.57	0.39
Mixed breed	2.49	0.78-8.00	0.12	2.79	0.73-9.89	0.12
Golden Retriever	4.81	0.58-40.22	0.15	3.85	0.46-32.31	0.21
Yorkshire Terrier	4.81	0.58-40.22	0.15	3.99	0.46-32.31	0.21
Sex (male vs. female)	0.97	0.49-1.90	0.92	0.94	0.46-1.95	0.87
Neuter Status (neutered vs. intact)	1.60	0.38-6.66	0.52	1.48	0.32-6.93	0.62
Diet						
HPHF v HPMF <sup>d</sup>	1.36	0.65-2.83	0.41	1.52	0.70-3.29	0.29
Dry v wet /mix	6.07	1.21-30.38	0.028	4.15	0.73-23.57	0.11
Concurrent hypothyroidism	1.96	0.20-19.37	0.56	1.57	0.16-15.55	0.70

Dirlotapide use	0.15	0.02-1.40	0.095	0.12	0.01-1.10	0.061
Rate of weight loss (per %/week)	3.35	1.35-8.30	0.0092	4.15	1.50-11.44	0.0061
Duration (per day)	1.003	1.000-1.004	0.014	1.002	1.000-1.004	0.046
Energy intake	0.99	0.95-1.03	0.49	0.98	0.94-1.02	0.37
Weight loss stalls (per stall)	0.90	0.78-1.05	0.17	0.87	0.74-1.02	0.092
Diet energy intake changes (per change)	1.11	0.95-1.29	0.19	1.08	0.93-1.27	0.31
Multiple regression						
Breed: Mixed breed	6.22	1.10-35.30	0.039			
Body Fat (per %)	0.87	0.80-0.94	< 0.001	0.88	0.81-0.96	0.0039
Diet: Dry v wet /mix	15.93	1.97-128.91	0.0095	15.37	1.57-150.71	0.019
Dirlotapide use	0.01	0.00-0.27	0.0031	0.02	0.00-0.43	0.011
Rate of weight loss (per %/week)	10.66	2.99-38.00	< 0.001	9.52	2.58-35.16	< 0.001
Duration (per day)	1.010	1.01-1.013	< 0.001	1.009	1.005-1.013	< 0.001

a: Odds Ratio, b: Confidence Interval, c: Cavalier King Charles Spaniel, d: High Protein Medium Fiber (Satiety) diet and High Protein High Fiber (Obesity dry diet).