YOUR **WEIGHT** TOOLKIT

Clinical Evidence

Clinical nutrition with proven results, backed by science. By conducting thorough research, Hill's is able to provide innovative nutritional solutions with the power to transform the lives of pets and the people who care for them.

Hogarth Worldwide

Project and Job Number **146710_1387381**	Client **Hills**		Type Area Box (h x w) –
Publication	Market **Multiple Markets**		Trim Box (h x w) **297.00 x 198.00 mm**
Insertion Date	Operator **Bogdan Cazacioc**		Bleed Box (h x w) **303.00 x 204.00 mm**
Contact **stefan.buda@hogarthww.com**		Revision	Date & Time **21/04/2017 11:06**

Operator	Proofreader
Line Manager	Account Manager
Light Box	Light Box

Cyan
Magenta
Yellow
Black

164 Shaftesbury Avenue, London WC2H 8HL +44(0)20 7240 6400 www.hogarthww.com

Hill's Evidence-Based Clinical Nutrition™

for Hill's™ Prescription Diet™ Metabolic Canine nutrition

WEIGHT LOSS

A REDUCED CALORIE, HIGH-FIBRE FOOD WITH ADDED COCONUT OIL, L-CARNITINE, LYSINE, AND LEUCINE INCREASES BASAL METABOLIC RATE IN OVERWEIGHT AND OBESE DOGS

Jewell D, Floerchinger A, Jackson M, *et al. J Vet Intern Med.* 2014;28(3):1087–1088:(NM-9).

KEY POINTS:

- Obese dogs lost 1.4% body weight per week during first four months.
- Compared to the start of the study, after four months of maintenance feeding, lean body mass increased 2.6%.
- Metabolic rate after weight loss appeared to increase as evidenced by preservation of body weight despite increased caloric intake compared with a control group.

EFFECTIVENESS OF A NEW WEIGHT MANAGEMENT FOOD TO ACHIEVE WEIGHT LOSS AND MAINTENANCE IN CLIENT-OWNED OBESE DOGS

Christmann U, Becvarova I, Werre S, Meyer H. *Intern J Appl Res Vet Med* 2015;13(2):104–116.

KEY POINTS:

- 94% of the dogs (n = 153) fed Hill's™ Prescription Diet™ Metabolic™ lost weight with an average weight loss of 14.5% over 6 months and an average weekly weight-loss rate of 0.73%.
- BCS and BFI decreased significantly over time compared to baseline.
- 55% of dogs ate more Hill's™ Prescription Diet™ Metabolic than the recommended DER for weight loss and 94% of these dogs still lost weight.
- Owners perceived a significant increase in energy and happiness in the dogs after weight loss without changes in appetite or begging behaviour, and significant improvements in dog's quality of life.†

WEIGHT MAINTENANCE

EFFECT OF FEEDING A WEIGHT LOSS FOOD BEYOND A CALORIC RESTRICTION PERIOD ON BODY COMPOSITION AND RESISTANCE TO WEIGHT GAIN IN DOGS

Floerchinger AM, Jackson MI, Jewell DE *et al. J Am Vet Med Assoc* 2015;247:375–384.

KEY POINTS:

- Overweight and obese dogs lost body weight and body fat mass, yet maintained most of their lean body mass when fed Prescription Diet™ Metabolic.
- Following the restricted intake period, dogs generally gained lean body mass and continued to lose body fat despite an increase in volume and caloric consumption to maintain body weight (Figure 1).
- In conclusion, feeding Metabolic to overweight dogs caused weight loss as well as improvements in body composition during the weight maintenance phase, possibly because the food composition improved energy metabolism.

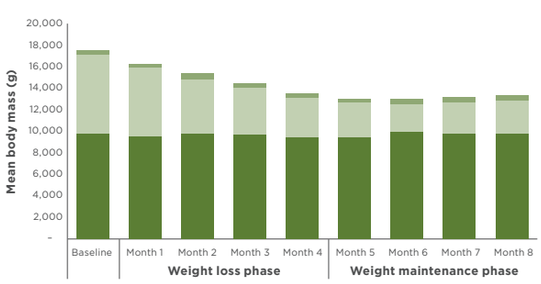

Figure 1: Mean body mass for 20 overweight or obese dogs fed Metabolic Canine.
Lean body mass (dark green bars), body fat mass (light green bars), and bone mass (green bars) were determined monthly by DEXA.

WEIGHT MANAGEMENT + JOINT CARE

GENERAL BACKGROUND

Forty percent of dogs with osteoarthritis (OA) are obese.[1] The biomechanical stress of excess weight is thought to be a primary contributor to the pathogenesis and progression of OA. In addition to the biomechanical stress, the constant low-grade inflammation associated with obesity may play a role in the development and progression of OA.[2,3]

Weight loss has been shown to improve the signs of OA in dogs.[4–13] Omega-3 fatty acids from fish oil provide clinical benefit by helping control inflammation and by reducing the expression and activity of cartilage proteoglycan-degrading enzymes.[14]

Hill's™ Prescription Diet™ Metabolic+Mobility has the nutritional attributes of Hill's™ Prescription Diet™ Metabolic and Hill's™ Prescription Diet™ j/d™Canine.

EFFECTIVENESS OF A NEW DIETETIC FOOD TO ACHIEVE WEIGHT LOSS AND TO IMPROVE MOBILITY IN CLIENT-OWNED OBESE DOGS WITH OSTEOARTHRITIS

Christmann U, Becvarova I, Werre S, Meyer H. *J Vet Intern Med* 2017;31:237 (ESVCN-O-5).

KEY POINTS:

- 89% of the overweight and obese dogs (n = 34) fed with Hill's™ Prescription Diet™ Metabolic+Mobility Canine dry lost weight over 6 months with an average weekly weight-loss rate of 0.5% of starting body weight.
- BCS and BFI decreased significantly over time compared to baseline.
- Owners perceived a significant improvement:
  - in rising and playing starting at month 2 of the study.
  - and in walking and activity level starting at month 3 of the study.
- Similarly, veterinarians' assessments revealed a significant improvement in lameness, weight bearing, and pain on palpation starting in month 3 of the study (Figure 2).
- In conclusion, owners and veterinarians reported significant improvements in dog's weight and mobility without negative side effects.

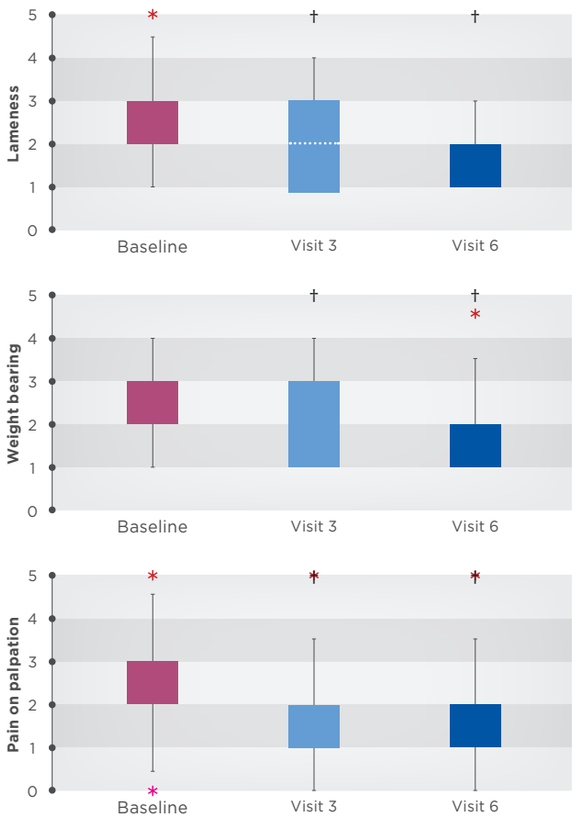

Figure 2: Veterinarians' assessment of osteoarthritis related parameters (data is presented as median and interquartile range. † $p < 0.05$ is significantly different from the baseline. * Min outlier * Max outlier)

REFERENCES

1. Banfield State of Health Report, 2012.
2. Eisele I, Wood IS, German AJ, *et al.* Adipokine gene expression in dog adipose tissues and dog white adipocytes differentiated in primary culture. *Horm Metab Res* 2005;37:474–481.
3. Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. *Br J Nutr* 2004;92:347–355.
4. Moreau M, Troncy E, Bichot S, *et al.* Influence of changes in body weight on peak vertical force in osteoarthritic dogs: a possible bias in study outcome. *Vet Surg* 2010;39:43–47.
5. Smith GK, Mayhew PD, Kapatkin AS, *et al.* Evaluation of risk factors for degenerative joint disease associated with hip dysplasia in German Shepherd Dogs, Golden Retrievers, Labrador Retrievers, and Rottweilers. *J Am Vet Med Assoc* 2001;219:1719–1724.
6. Huck JL, Biery DN, Lawler DF, *et al.* A longitudinal study of the influence of lifetime food restriction on development of osteoarthritis in the canine elbow. *Vet Surg* 2009;38:192–198.
7. Runge JJ, Biery DN, Lawler DF, *et al.* The effects of lifetime food restriction on the development of osteoarthritis in the canine shoulder. *Vet Surg* 2008;37:102–107
8. Smith GK, Paster ER, Powers MY, *et al.* Lifelong diet restriction and radiographic evidence of osteoarthritis of the hip joint in dogs. *J Am Vet Med Assoc* 2006;229:690–693.
9. Kealy RD, Lawler DF, Ballam JM, *et al.* Evaluation of the effect of limited food consumption on radiographic evidence of osteoarthritis in dogs. *J Am Vet Med Assoc* 2000;217:1678–1680.
10. Kealy RD, Olsson SE, Monti KL, *et al.* Effects of limited food consumption on the incidence of hip dysplasia in growing dogs. *J Am Vet Med Assoc* 1992;201:857–863.
11. Marshall WG, Hazewinkel HA, Mullen D, *et al.* The effect of weight loss on lameness in obese dogs with osteoarthritis. *Vet Res Commun* 2010;34:241–253.
12. Mlacnik E, Bockstahler BA, Muller M, *et al.* Effects of caloric restriction and a moderate or intense physiotherapy program for treatment of lameness in overweight dogs with osteoarthritis. *J Am Vet Med Assoc* 2006;229:1756–1760.
13. Kirkby KA, Lewis DD. Canine hip dysplasia: reviewing the evidence for nonsurgical management. *Vet Surg* 2012;41:2–9.
14. Caterson B, Flannery CR, Hughes CE, *et al.* Mechanisms involved in cartilage proteoglycan catabolism. *Matrix Biology* 2000;19:333–344.

Hill's Evidence-Based Clinical Nutrition™

The nutrition in Prescription Diet™ Metabolic+Urinary Stress effectively reduces body weight and helps manage cats with feline idiopathic cystitis (FIC)

KEY POINTS:

The nutrition in Hill's™ Prescription Diet™ Metabolic+Urinary Stress Feline:

- **Is clinically proven to support a mean weight loss of 11% in 60 days**
- **Reduces the recurrence of FIC signs by 89%**
- **Contains milk protein hydrolysate (hydrolysed casein) and L-tryptophan to help control stress**

INTRODUCTION

Feline Lower Urinary Tract Disease (FLUTD) signs, including pollakiuria, dysuria, haematuria, periuria and/or stranguria, may occur with urolithiasis; however, no underlying cause can be found in 60% of cases and it is called feline idiopathic cystitis (FIC).[1] Being overweight or obese is associated with a 3-fold increase in prevalence of FLUTD signs.[2] Current evidence suggests that stress also plays an important role in the pathogenesis of FIC[3] and it has been shown that reducing stress by environmental enrichment significantly decreases the clinical signs of FIC.[4] Nutritional intervention has been shown to effectively manage obesity and reduce recurrence of FLUTD signs in cats. Nutritional interventions for concurrent weight loss and management of FLUTD are available in a single product, Prescription Diet™ Metabolic+Urinary Stress Feline (Figure 1).

SECTION 1
NUTRITIONAL MANAGEMENT OF WEIGHT

Previous studies in overweight cats evaluated foods that contain the nutrition of Prescription Diet™ Metabolic.[5,6] Results of one of the studies have been published in the *Journal of the American Veterinary Medical Association* (JAVMA). Overweight was defined by BCS 4 or 5; > 30% body fat as determined by DEXA for standardisation.

Study 1 - published in JAVMA
20 overweight cats were enrolled and assigned to a test food containing the nutrition found in Prescription Diet™ Metabolic Feline.

Study 2
13 overweight cats were enrolled and assigned to a test food containing the nutrition found in Prescription Diet™ Metabolic Feline.

METHODS

Control and test foods for both studies met or exceeded Association of American Feed Control Officials' (AAFCO) guidelines for complete and balanced nutrition for maintenance of adult cats. Cats in both test groups were initially fed at least 0.8*RER (resting energy requirement) of estimated ideal body weight. All cats were weighed weekly with food intake monitored daily and adjusted every two weeks if necessary to target a safe rate of weight loss (0.5–1.0% body weight/week).[7]

The 20 cats in the JAVMA study stayed on a weight loss regimen until they had reached an ideal body condition or four months, whichever occurred first, followed by a 4-month weight maintenance period. During weight maintenance, they were fed to maintain the body weight achieved at the end of the weight loss period. DEXA analysis for study 1 was performed monthly throughout the study.

The cats in study 2 continued a weight loss regimen until they reached an ideal body condition or eight months, whichever occurred first, and DEXA scans were done monthly. The weight loss phase was followed by a 6-month weight maintenance phase with DEXA scans performed every second month.

RESULTS

Weight loss (*combined groups*)
Cats in both studies fed the nutrition of Prescription Diet™ Metabolic lost weight and had no weight loss-related adverse events reported. Significant weight loss was observed after 60 days on the weight loss regimen. Cats safely exceeded recommended weight loss 0.5–1.0%[7] of body weight per week for the combined study results over 60 days. This translated to an average weight loss over 60 days of 14.5% and 7.6% in studies 1 and 2, respectively.

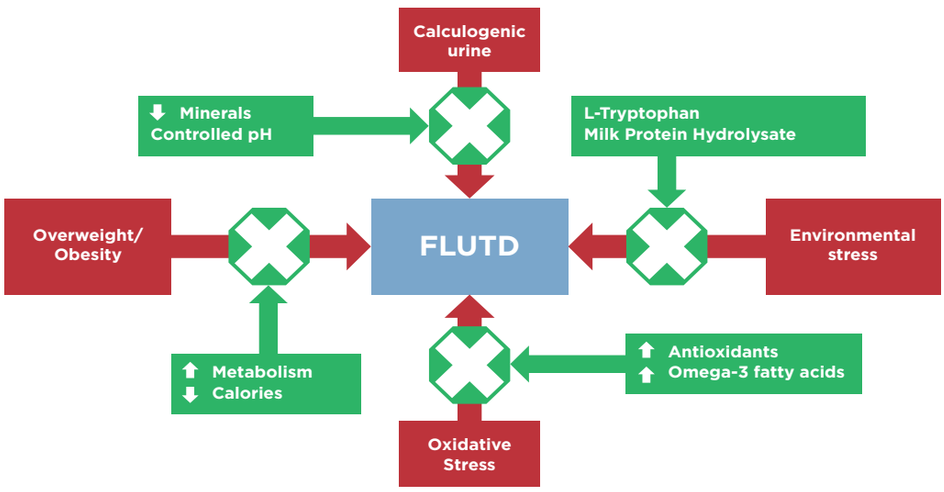

Figure 1: Metabolic+Urinary Stress contains four distinct nutritional technologies to help manage overweight/obesity (synergistic blend of ingredients), stress (L-tryptophan and alpha-casozepine), calculogenic urine (controlled minerals and urine pH) and oxidative stress (antioxidants).

Weight maintenance

In addition, the published JAVMA results revealed that cats in the weight maintenance phase of the study consumed more calories than colony controls to maintain body weight, thus resisting weight regain. DEXA analysis during the weight maintenance period revealed that cats continued to lose significant amounts of fat mass while adding significant amounts of lean mass without a change in overall weight.[5]

Study 3

This clinical study confirmed the effectiveness of Prescription Diet™ Metabolic in achieving weight loss in overweight/obese client-owned cats in spite of a higher than recommended caloric intake. Owners reported significant improvements in their cat's quality of life specifically in regard to perceived levels of energy and happiness, without negative side effects such as changes in appetite or begging behavior.[8]

SECTION 2
NUTRITIONAL MANAGEMENT OF FIC

Recently published in JAVMA, results of a study have shown that the nutrition of Prescription Diet™ c/d™ Multicare Feline reduced recurrent episodes of FIC signs.[3]

PURPOSE

To evaluate the efficacy and safety of a dietetic urinary food for decreasing recurrent episodes of FIC signs.

DESIGN

Male or female neutered cats with clinical signs of FIC were recruited for the study at Michigan State University and the University of Minnesota. Cats lived indoors and ranged in age from 1–8 years, and were considered for inclusion in the study if they had experienced an acute episode of ≥ 2 lower urinary tract signs (haematuria, dysuria, stranguria, pollakiuria and/or periuria) in the past 7 days. Owners could choose whether they wanted to offer wet or dry food exclusively and then cats were assigned randomly to either the test or control food groups. Investigators and pet owners were masked to treatment groups for the duration of the 12-month study. The test food was commercially available c/d™ Multicare Feline formula. The control food was formulated to meet or exceed AAFCO requirements for adult cats, with mineral concentrations and target urine pH designed to mimic common selling grocery brands. Compared with the control food, the test food contained substantially higher concentrations of antioxidants and Omega-3 fatty acids.

The primary endpoint measured was the number of recurrent episodes of FIC signs within 12 months. A recurrent episode of FIC was defined as the presence of ≥ 2 clinical signs (haematuria, dysuria, stranguria, pollakiuria and/or periuria) on a single day. An episode was considered to have resolved when there were two consecutive days with ≤ 1 clinical sign.

Owners were instructed to return to the veterinary hospital should a recurrence of clinical signs occur and also for scheduled rechecks at 1, 3, 6, 9 and 12 months. At the end of the 12-month study, cats returned to the veterinary hospital for a physical examination, urinalysis, urine culture, serum chemistries and diagnostic imaging of the lower urinary tract.

RESULTS

A total of 25 cats were included in the study with 11 cats in the test food group and 14 cats in the control food group. There was no statistical difference in recurrence of lower urinary tract signs between the dry and wet formulations; therefore, data from cats in the dry and wet groups were combined and comparisons were made between nutritional profiles (test food vs. control food).
Cats consuming the test food had a significantly lower proportion of total days with ≥ 2 clinical signs and total episodes of FIC signs ($P < 0.05$) with 4/11 (36%) test food group cats and 9/14 (64%) control food group cats exhibiting ≥ 2 clinical signs on at least one occasion during the 12-month study.

At least two clinical signs were observed on any particular day 13 times in the test food group and 152 times in the control food group. The rate of recurrent episodes of FIC signs was 5/3904 days (1.28/1,000 cat-days) in the test food group and 47/4,215 days (11.15/1,000 cat-days) in the control food group. This represents an 89% reduction in the rate of recurrent episodes of FIC signs in cats fed the test food (c/d™ Multicare Feline) consistently for 12 months compared with the control food group (Figure 2).

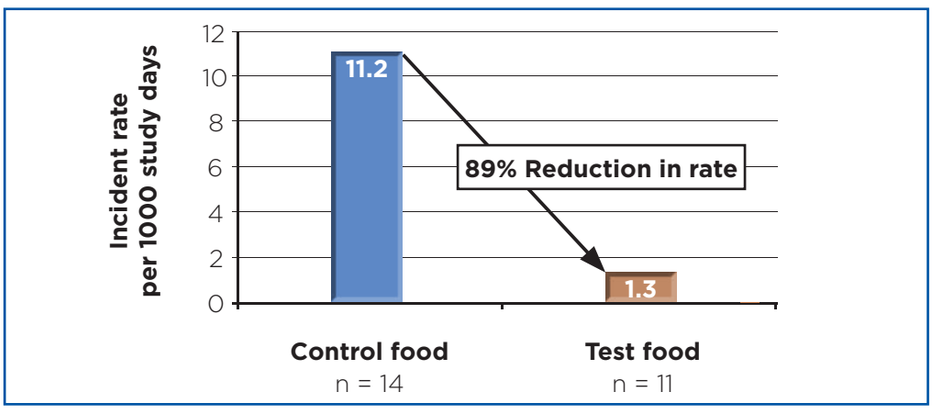

Figure 2: Significant reduction in the rate of recurrent episodes of FIC signs.

CONCLUSIONS AND CLINICAL RELEVANCE

This is the first study to definitively show that foods of different nutritional profiles impact the expression of acute FIC signs in cats.

SUMMARY

Investigators determined that consistent feeding of c/d™ Multicare to cats with FIC resulted in decreased recurrence of episodes of FIC signs during a 12-month randomised, controlled, double-blinded clinical study, published in JAVMA.

SECTION 3

NUTRITIONAL MANAGEMENT OF STRESS

Oral supplementation with L-tryptophan (an essential amino acid) and alpha-casozepine (a milk protein hydrolysate or hydrolysed casein) have been reported to have positive effects on alleviating anxiety and stress-related behaviours in various species including cats[9–12] and may, therefore, aid in the management of FIC.

EFFECTS OF A URINARY FOOD SUPPLEMENTED WITH MILK PROTEIN HYDROLYSATE AND L-TRYPTOPHAN ON FELINE IDIOPATHIC CYSTITIS[13]

STUDY DESIGN

A blinded, uncontrolled study of 10 cats with FIC was conducted to evaluate the effects of a urinary food supplemented with milk protein hydrolysate and L-tryptophan.

Cats (mean age 5.9 years) were diagnosed with FIC by ruling out other causes of FLUTD. Cats with other major diseases and/or receiving medical treatment that could affect their stress levels were excluded from the study. A thorough history was taken related to dietary intake and environmental enrichment of the cat. After enrolment the cats were transitioned to a urinary food supplemented with milk protein hydrolysate and L-tryptophan (Prescription Diet™ c/d™ Urinary Stress, dry and/or pouches) at home. Advice was given as to how to improve the environment following a protocol described by Buffington *et al.*[14]

Cat emotional scores, quality of life and FLUTD scores (including overgrooming) were recorded at enrolment and during clinic visits after four and eight weeks. Taste perception of the new food was recorded during repeat visits. These data were also recorded during telephone interviews by the practice at two and six weeks after enrolment.

RESULTS

- Taste perception of both the dry and wet formulas was rated as excellent throughout the study.
- Emotional scores and quality of life, as perceived by the owner, improved significantly on the new food (Figure 3).
- FLUTD signs also improved significantly as rated by the owners (Figure 4).

CONCLUSION AND CLINICAL IMPORTANCE

The results of this study provide provisional evidence that a urinary food supplemented with milk protein hydrolysate and L-tryptophan (Hill's™ Prescription Diet™ c/d™ Urinary Stress) significantly reduces FLUTD and improves emotional scores and quality of life in cats with FIC. Because stress is believed to play an important role in the pathogenesis of FIC, managing both stress and FLUTD may act synergistically.

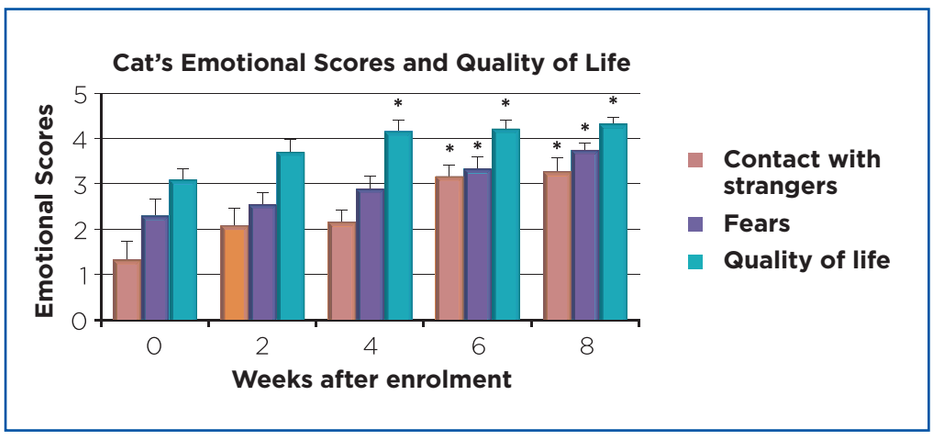

Figure 3: Cat emotional scores and Quality of Life (mean ± SEM) in 10 cats with FIC at week 0 (enrolment), 2, 4, 6 and 8.

* denotes significant difference ($p < 0.05$) vs. week 0. Emotional scores are on a 6-point ordinal scale (0 – high anxiety levels to 5 – low anxiety levels). The cat emotional score system is adapted from Beata *et al.*[12] Quality of Life is rated on a 5-point ordinal scale (1 – very poor to 5 – excellent).

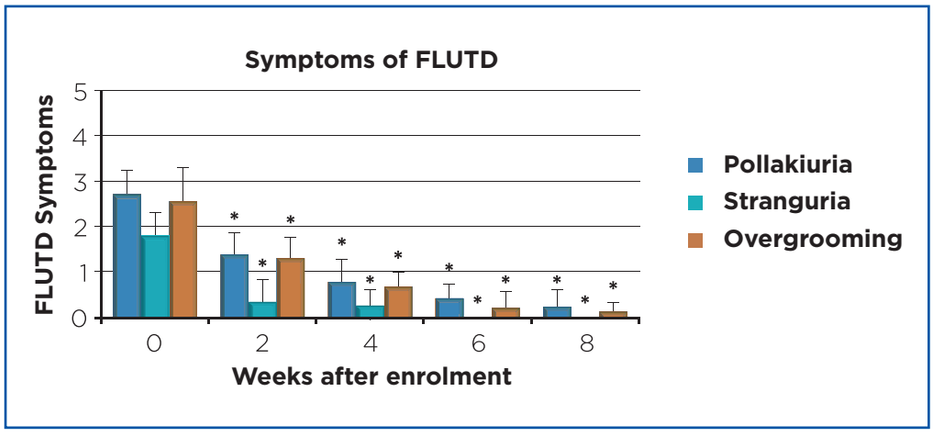

Figure 4: FLUTD scores (mean ± SEM) in 10 cats with FIC at week 0 (enrolment), 2, 4, 6 and 8.

* denotes significant difference ($p < 0.05$) vs. week 0.
All scores are on a 6-point ordinal scale (0 – no presence to 5 – severe presence).

SCIENTIFIC INSIGHTS SUMMARY

Weight and stress are postulated to play an important role in the development of FIC. In addition, excessive nutrients such as magnesium or phosphorus also contribute to urolithiasis. Managing the most difficult and complex FLUTD cases is made simple with one comprehensive, clinically-proven nutrition: Prescription Diet™ Metabolic+Urinary Stress Feline.

REFERENCES

[1] Lekcharoensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Assoc* 2001;218:1429–35.

[2] Lund EM, Armstrong PJ, Kirk CK, Klausner JS. Prevalence and risk factors for obesity in adult cats from private US veterinary practices. *Intern J Appl Res Vet Med* 2005;3:88–96.

[3] Kruger JM, Lulich JP, Merrills J, *et al.* Comparison of foods with differing nutritional profiles for long-term management of acute nonobstructive idiopathic cystitis in cats. *J Am Vet Med Assoc* 2015;247(5):508–517.

[4] Westropp JL, Buffington CAT. Feline idiopathic cystitis: Current understanding of pathophysiology and management. *Vet Clin N Am Small Anim Pract* 2004;34:1043–1055.

[5] Floerchinger AM, Jackson MI, Jewell DE *et al.* Effect of feeding a weight loss food beyond a caloric restriction period on body composition and resistance to weight gain in cats. *J Am Vet Med Assoc* 2015;247:365–374.

[6] Data on File. Hill's Pet Nutrition, Inc. Topeka, KS.

[7] Toll PW, Yamka RM, Schoenherr WD, Hand MS. Obesity. In: Hand MS Thatcher CD, Remillard RL, Roudebush P, Novotny BJ, eds. Small Animal Clinical Nutrition, 5th ed. Topeka, KS: Mark Morris Institute; 2010;502–541.

[8] Christmann U, Becvarova I, Werre S, Meyer H. Effectiveness of a new dietetic weight management food to achieve weight loss in client-owned obese cats. *J Feline Med Surg* 2016;18(12):947–953.

[9] Pereira GG, Fragoso S, Pires E. Effect of dietary intake of L-tryptophan supplementation on multi-housed cats presenting stress related behaviors (abstr), in proceedings. British Small Animal Veterinary Association, April 2010.

[10] Batool F, Ahmed S, Haleem DJ. Dietary supplementations of amino acids: Evidence for enhanced serotonergic functions following haloperidol withdrawal in rat medial prefrontal cortex. *Coll Physicians Surg Pak* 2009;19:139.

[11] Miclo L, Perrin E, Driou A, *et al.* Characterization of alpha-casozepine, a tryptic peptide from bovine alpha-s1-casein with benzodiazepine-like activity. *Fed Am Soc Exp Biol Journal* 2001;10:1780–1782.

[12] Beata C, Beaumont-Graff E, Coll V, *et al.* Effect of alpha-casozepine (Zylkene) on anxiety in cats. *J Vet Behaviour* 2007;2:40–6.

[13] Meyer HP, Becvarova I. Effects of a urinary food supplemented with milk protein hydrolysate and L-tryptophan on feline idiopathic cystitis – Results of a case series in 10 cats. *Intern J Appl Res Vet Med* 2016;14(1):59–65.

[14] Buffington CAT, Westropp JL, Chew DT, *et al.* Clinical evaluation of multimodal environmental modification (MEMO) in the management of cats with idiopathic cystitis. *J Feline Med Surg* 2006;8:261–268.

Clinical Evidence

Our mission is to help enrich and lengthen the special relationships between people and their pets. We firmly believe that the right pet nutrition is vital to pets' living long, healthy lives. Backed by extensive Evidence-Based Clinical Nutrition, we are proud to use the latest in cutting-edge food science to create clinical nutrition with the power to transform lives.