Simple Nutritional Solutions for Complicated Cases

Todd L. Towell, DVM, MS, DACVIM

Abstract

Obesity has consistently been identified as a risk or exacerbating factor for a variety of comorbid conditions. There is no doubt that obesity in both human and pet populations has reached epidemic proportions. This has led to the rise of pets with concurrent conditions. It is common to be presented with pets that are diagnosed with obesity AND another condition. In dogs this is most often obesity AND osteoarthritis (OA), for cats lower urinary tract signs (LUTS) AND obesity is a common occurrence. This presents a challenge for the veterinary health care team when making a specific nutritional recommendation. Historically you had to decide which condition would benefit most from nutritional management, obesity OR OA; obesity OR LUTS. The introduction of Hill's® Prescription Diet® Metabolic Plus Mobility and Hill's® Prescription Diet® Metabolic Plus Urinary means pets can now benefit from the power of AND. Specific nutritional recommendations can now be customized for the specific needs of each individual pet, simplifying management for the pet, pet owner and the entire veterinary health care team.
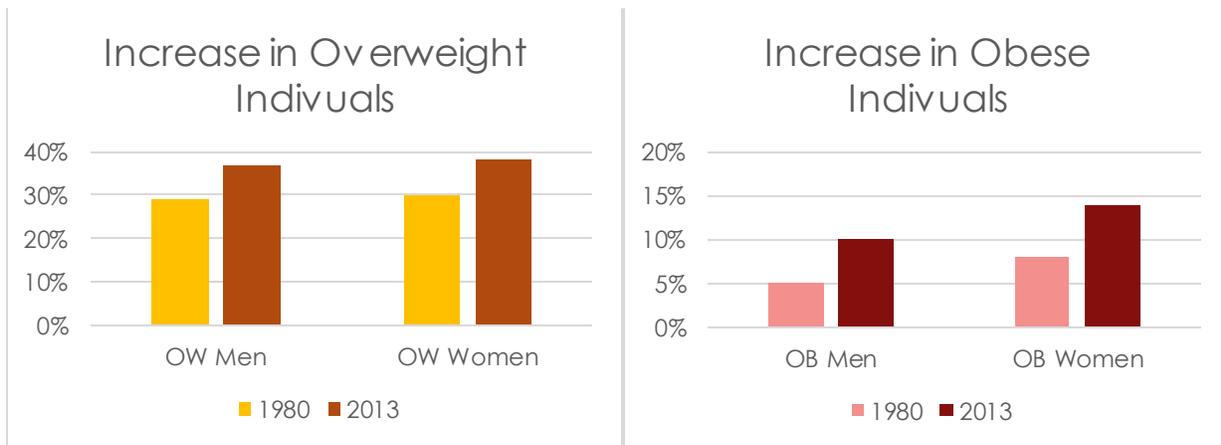
Global Obesity Trends: Human Perspective

Over one third of the global human population (~37% of men and 38% of women) were classified as overweight (Body Mass Index (BMI) >25- 30) or obese (BMI >30) in 2013. Simply put, the world is fat. As little as 20 years ago hunger was the most common form of malnutrition in developing countries.
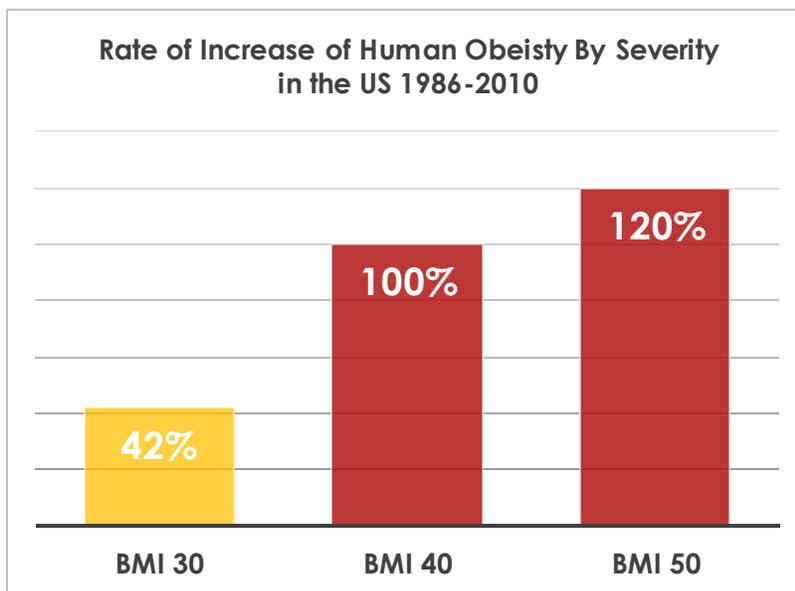
Today, over half (65%) of the world's population live in countries where consequences of being overweight or obese kills more people than consequences of being underweight.[1]

While the rate of increase in all overweight individuals is growing by single digits, ~ 8% over the last three decades, the increase in obese individuals is skyrocketing. Globally,

the prevalence of obese (BMI > 30) individuals has essentially doubled in both men and women since the 1980's.[2,3]

Increase in Overweight Indivuals

40%	
30%	
20%	
10%	
0%	
	OW Men OW Women

■ 1980 ■ 2013

Increase in Obese Indivuals

20%	
15%	
10%	
5%	
0%	
	OB Men OB Women

■ 1980 ■ 2013

Among developed countries, the United States stands out for its high prevalence of obesity (BMI > 30). In 2013 roughly one third of adult men (~32%) and women (~34%) were classified as not just overweight but obese.[2] As a result of the increasing severity of this disease, new diagnostic tools have been developed to aid human health care providers. When the BMI scale was initially validated patients were classified as underweight (BMI< 18.5), normal weight (BMI18.5 – 25), overweight (BMI >25 – 30) and obese (BMI > 30). In recent years it has become necessary for human health organizations to expand this scale to describe the increasing severity of this disease. Obesity is now categorized as Class I (BMI 30-35), Class II (35-40) and Class III (BMI > 40). While most reports still categorize all patients with BMI > 30 as obese, this broad classification obscures the heterogeneity of disease. A recent meta-analysis documents significantly

Rate of Increase of Human Obeisty By Severity in the US 1986-2010

BMI 30	BMI 40	BMI 50
42%	100%	120%

higher hazard ratios for all-cause mortality in patients with grades 2 and 3 obesity relative to normal weight patients.[4] Unfortunately, two recent reports document that the population of severely obese patients in the US is increasing.[5,6] While the rate of increase in the prevalence of overweight/mildly obese patients (BMI 25-39) may be

slowing, in the last 25 years the rate of increase in patients with BMI of 40 and 50 has increased 100% or more. Not only are more people overweight, particularly in the US, the severity of this disease continues to increase at alarming rates.

Global Obesity Trends: Pet Perspective

**DOGS 1983**

(pie chart: Obese, Thin, OW, Normal)
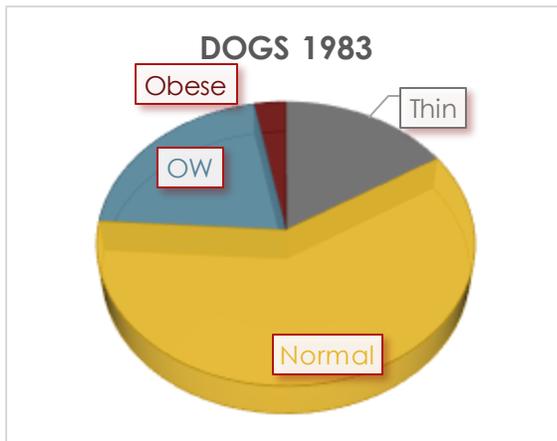
During the same decades that saw the emergence of overweight and obesity as an epidemic in humans a similar trend in has been developing in our pets. The global incidence of overweight and obese pets has steadily increased since the 1980's. Current estimates suggest that globally over 50% of pets are overweight or obese.[7-13] This trend coincides with changing attitudes about pets and the move from 'the barn to the bedroom'.

DOGS 2013

(pie chart: Thin, Obese, Normal, OW)
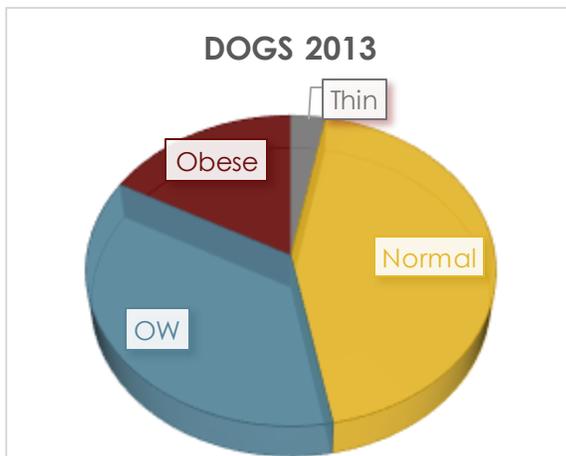
In the past three decades the percent of dogs considered overweight has increased from approximately 20% to 36%. Like the human population, there has been a dramatic increase in dogs considered obese, climbing from a mere 3% of dogs in 1983 to almost 20% in 2013.[14,15] For cats, this same trend has been documented over the past two decades. In 1994 over 60% of cats were considered normal body condition and only 1% obese.[16] Today 60% of cats are overweight (OW) or obese. Most alarming is the dramatic increase in obese cats (5/5 body condition score) which is now almost 30%.[15]

CATS 1994

(pie chart: Obese, OW, Thin, Normal)

CATS 2013

(pie chart: Thin, Obese, Normal, OW)
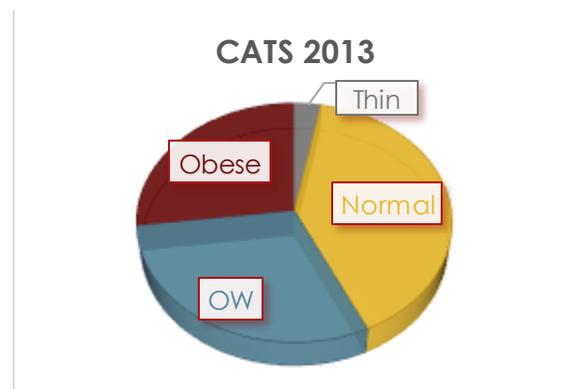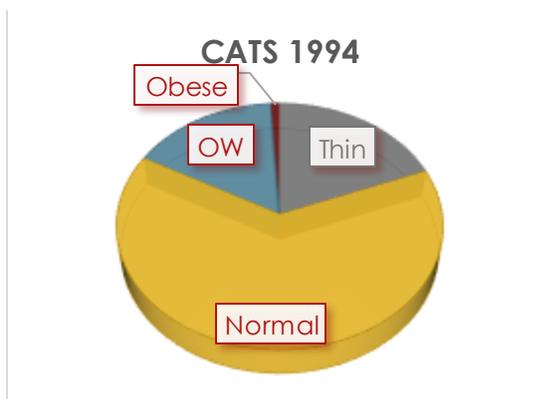
Like human health organizations if has become necessary for the veterinary profession to incorporate new tools to describe this new population of increasingly obese pets. Researchers at the University of Tennessee and Hill's Pet Nutrition have developed two new tools to more accurately determine body composition and estimate ideal body weight in overweight and obese pets. These methods were developed and validated in a population of pets that reflects the current heterogeneity of the disease. These studies included pets with 25 to over 60% body fat.[17,18] These newly described tools, the Body Fat Index and Morphometric Measurements, are collectively referred to as The Hill's Healthy Weight Protocol tools and can be accessed online at http://www.hwp.hillsvet.com.

Prior to the introduction of these new tools; the most commonly used method of assessing body composition in clinical practice was body condition scoring (BCS 5 or 9 point scales). Similar to BMI in humans, BCS methods were validated in populations that did not include pets with greater than ~ 45% body fat.[19-21] Incorporation of the Healthy Weight Protocol tools by general practices across North America from 2012 to 2014 has provided insight into the current state of obesity in pets. Preliminary evaluation of data from online data for over 56,000 feline entries, ~ 33,000 evaluated by the Morphometric Measurement method and ~ 23,000 evaluated by the Body Fat Index method confirm that like people, the severity of this disease is increasing in our pets. The distribution of body composition of overweight cats illustrates the magnitude of the problem. A similar trend is evident in data (not shown) from dogs assessed using these new tools.

Distribution of Overweight Cats by % Body Fat Category
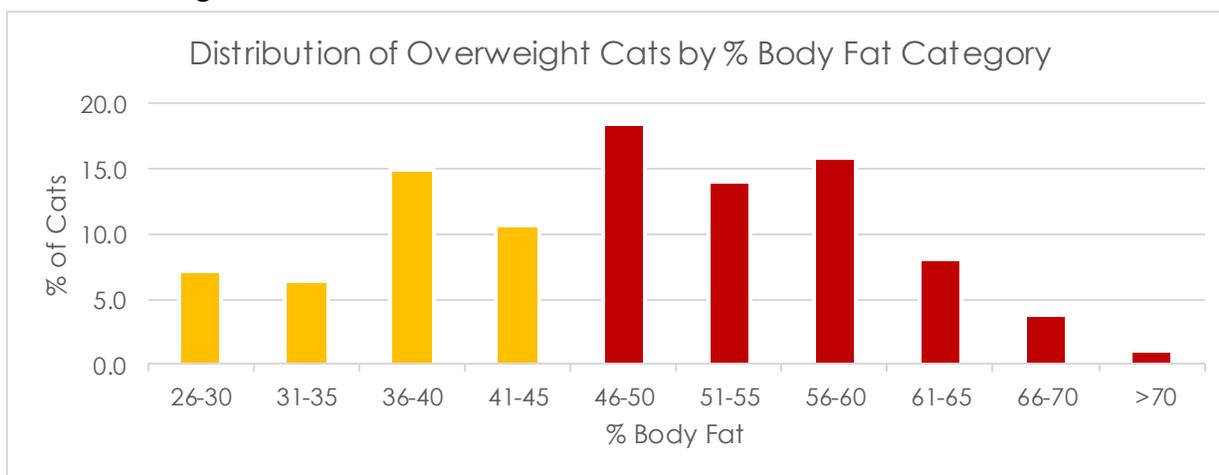
Over 60% of overweight cats evaluated with the Hill's Healthy Weight Protocol tools in veterinary practices across the US and Canada have greater than 45% body fat.

Consequences of Abnormal Body Composition: Canine

In human medicine the massive burden of obesity and its related disease cluster are now leading global public health problems.[22] Excess adipose tissue has been linked to an increased risk of morbidity from numerous pathologies, from periodontal disease to chronic kidney disease, kidney stones, hypertension, dyslipidemia, type 2 diabetes, coronary heart disease, stroke, non-alcoholic fatty liver disease, osteoarthritis, sleep apnea, and endometrial, breast, prostate, and colon cancers.[23-27] In pets, obesity has been associated with insulin resistance/ diabetes mellitus, lameness, osteoarthritis (OA), dermatopathy, lower urinary tract disease, cardiovascular and renal disease, pancreatitis and shortened life span.[28] Similar to reports of increased all-cause mortality in humans, excess weight also adversely affects the overall health of pets. The trend of increasing severity of obesity in pets is particularly disturbing in light of evidence that indicates even moderately overweight dogs are at greater risk for earlier morbidity. A lifelong study in two groups of Labrador retrievers documented that the median lifespan of overweight dogs was approximately 2 years shorter than normal weight dogs.[29] In addition the overweight dogs required medication for osteoarthritis and other chronic health problems about 3 years sooner than their normal weight siblings.[29] These adverse effects occurred despite the fact that the overweight dogs only weighed about 26% more than the normal dogs. The average body condition score for the overweight dogs was 7 / 9 which equates to approximately 35% body fat.[20]
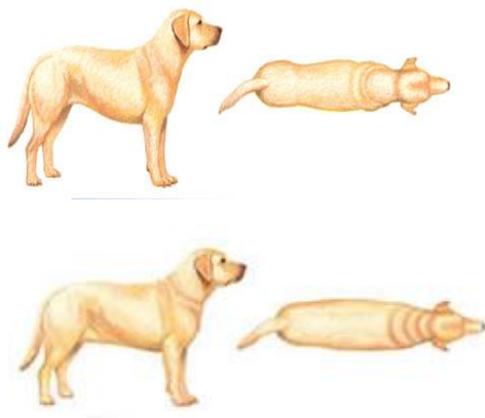
Approximate Body Condition (4-5/9) of Lean Fed Dogs with longer, healthier lives.

Approximate Body Condition (7/9) of Overweight dogs with shorter lives and more health problems.

Common Concurrent Conditions: Canine Osteoarthritis and Obesity

Osteoarthritis and obesity are perhaps the most common comorbid conditions veterinary health care professionals must manage. The biomechanical stress of excess weight is thought to be a primary perpetrator of the pathophysiology and progression of osteoarthritis.[30-33] Compared to normal weight dogs, obese dogs exert greater shear and compressive forces on many weight bearing joints. These increased forces may

explain the more rapid progression of osteoarthritis in obese dogs particularly in joints with intrinsic laxity where subluxation would be exacerbated.[32] Long before overweight dogs have clinical signs of lameness or radiographic signs of arthritis there are changes occurring at the level of the chondrocytes. One study demonstrated that even in the absence of any clinical signs overweight dogs had elevated markers of arthritis compared to a population of lean dogs.[34] These changes were not age related since the average age of lean dogs was 8.3 years and the average age of obese dogs was 6.7 years.

Indeed several studies document increased body weight / body condition score as risk factors for development of osteoarthritis in dogs with hip dysplasia and cranial cruciate ligament rupture (CCLR).[35-41] Evaluation of dogs diagnosed with CCLR in the Veterinary Medical Database (VMDB) from veterinary medical teaching hospitals in North America from 1967 – 1987 documented that compared to controls affected dogs were heavier and that Rottweilers were one of the 3 most commonly affected breeds.[42] A more recent study documents that overweight dogs are more likely to have bilateral rupture and Rottweilers also had the highest odds of bilateral rupture.[43] Interestingly, in the 2012 Banfield data, overweight was one of the three most common diagnoses in Rottweilers.[44]

In 2013 US based Veterinary Pet Insurance claims data documented arthritis as the 5th most common condition in dogs, up from the 6th most common claim in 2012. In England degenerative joint disease was the 5th and obesity the 7th most common diagnoses in an analysis of ~ 4,000 randomly selected records from a database of over 140,000 dogs presented to 93 primary care clinics from 2009- 2013.[45] In fact, the overall prevalence of arthritis in 2.3 million dogs evaluated in the US at Banfield hospitals has steadily increased from 2011 to 2014 and the condition is now diagnosed in 16% of all dogs presented for evaluation. [9,44,46,47] This is similar to the 15% total prevalence of hip dysplasia, a common cause of osteoarthritis, reported in ~ 34,000
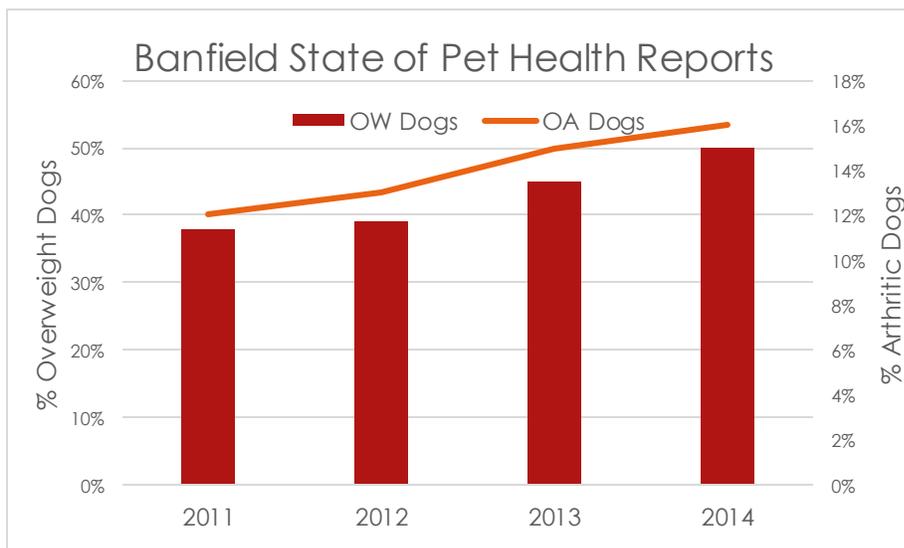
Banfield State of Pet Health Reports

dogs screened in the Netherlands from 2002 to 2010.[48] While the prevalence of hip dysplasia is decreasing in some breeds, a recent survey of radiographs submitted for evaluation from 2000-2006 for 31 breeds in France documented prevalences ranging from ~ 4% (Siberian Husky) to ~ 35% (Berger Picard).[49] As might be expected, in the 5 year period from 2007 and 2012 Banfield reported increases in both the diagnosis of overweight (37%) and arthritic (38%) dogs.[44] Not surprisingly 40% of dogs with arthritis are also overweight.[9]

While the effects of biomechanical stress of excess weight on arthritic joints is well recognized, the role obesity-associated systemic factors play is just beginning to be elucidated. It is increasingly clear that OA is both a degenerative and inflammatory condition which ultimately results in loss of cartilage matrix and organ failure. In humans obesity acts as a risk factor for both weight-bearing joints and nonweight-bearing joints, suggesting that obesity-associated systemic factors are involved in the pathogenesis of OA[50,51] Apidocytes secrete several hormones including leptin and adiponectin and produce a diverse range of adipokines. Among the currently recognized adipokines are a growing list of mediators of inflammation; TNF a, IL-6, IL-8, IL-10. These adipokines have been documented in both human and canine adipocytes.[52,53] Production of these proteins is increased in obesity suggesting that obesity is a state of chronic low-grade inflammation. The presence of low-grade inflammation may contribute to the pathophysiology of a number of diseases commonly associated with obesity including osteoarthritis. This might explain why relatively small reductions in body weight can result in significant improvement in clinical signs in arthritic patients.[54,55]

Nutritional Management: Osteoarthritis and Obesity

In human medicine obesity is recognized as such a strong independent risk factor for OA that strategies to reduce the obesity pandemic are considered key to reducing the prevalence of OA.[56] There is also growing evidence that the presence and magnitude of obesity affects response to therapies intended to control pain and improve function. A study designed to evaluate the relationship between BMI and pain and function in OA patients undergoing medical treatment found that the higher the initial BMI, the lower the improvement in pain (p = 0.03) and that function improved in inverse ratio to the initial BMI.[57] The authors conclude BMI determines how patients will respond to therapies. Another study also supports that severity of obesity directly influences the response to management. In a study of patients with knee OA, as body weight increased from overweight to class III obesity meaningful differences were noted in measures of mobility performance, mobility-related self-efficacy, pain symptoms, and measures of accelerometer-determined physical activity.[58] Normal weight patients

outperformed all other weight classes with respect to these assessments. Additionally, BMI has been found to be significantly associated with decreased quality of life (QOL) measures among adults with arthritis.[59] In this study BMI was associated with greater impairments in both physical function and QOL related measures, even after controlling for age, gender, race, self-reported moderately vigorous physical activity, and arthritis medication use, which supports the robustness of these relationships.[59] While weight loss is recommended for all overweight patients with arthritis, until recently many human health care providers believed that patients with severely affected joints would not benefit significantly from weight loss and were therefore reluctant to discuss this stigmatized and often difficult topic with patients. Results of a study designed to assess

"There is strong evidence for recommending weight loss as the first choice of treatment for obese patients with osteoarthritis"

how the pre-treatment structural status of the knee joint influenced symptomatic changes after weight loss indicate that any obese patient, whatever the level of knee damage, may benefit from a weight-loss program.[60] These benefits were seen after 16 weeks of dietary intervention in which the majority of patients obtained a weight reduction of > 10% of starting body weight. The authors conclude there is strong evidence for recommending weight loss as the first choice of treatment for obese patients with osteoarthritis of the knee regardless of the degree of structural damage present at diagnosis.

Overweight dogs with osteoarthritis present a unique challenge. Certainly using a multimodal approach to the management of dogs with OA improves chances of successfully disrupting the arthritis cycle and at the same time minimizing the use or dose of drugs necessary to control clinical signs. As with human OA patients, controlling weight in pets with OA or those at risk for developing OA is an effective method of decreasing the severity and delaying the onset of clinical signs.[33,36,55,61-68]

Indeed, noticeable improvement may be seen after modest weight loss (~ 6- 8) body weight.[66] However, at the same time a systematic review of all controlled *in vivo*

Among nutraceuticals, the highest global strength of evidence for efficacy controlling pain and improving gait was demonstrated by omega-3 fatty acid supplemented diets, specifically Hill's Prescription Diet® j/d® canine.

studies published prior to December 2010 evaluating the efficacy of supplements, foods, or natural substances to improve clinical signs of pain and abnormal gait in dogs with supports the use of foods supplemented with omega-3 fatty acids.[69] In this systematic review, of the 22 studies which met inclusion criteria only four were found to provide credible evidence for managing dogs with OA. Hill's Prescription Diet® j/d® canine was the omega-3 fatty acid supplemented diet evaluated in these four studies.[70-73] Based on this systematic review the authors concluded that "The highest global strength of evidence of efficacy was demonstrated by omega-3 fatty acid supplemented diets".[69]

The mechanisms of action of omega-3 fatty acids, specifically eicosapentaenoic acid (EPA) in the dog include controlling inflammation and reducing the expression and activity of cartilage degrading enzymes.[74] In vitro studies have documented that eicosapentaenoic acid (EPA) is selectively stored in canine chondrocytes. As a result, EPA replaces arachidonic acid in the inflammatory cascade significantly reducing the production of pro-inflammatory mediators. Reducing the production of proinflammatory mediators is one mechanism by which omega-3 fatty acids promote the termination of inflammation and the return to homeostasis. Research has demonstrated that resolution of inflammation is an active, endogenous process controlled in part by lipid mediators derived from omega-3 fatty acids, resolvins and protectins .[75] These bioactive mediators have potent antiinflammatory, neuroprotective and pro-resolving properties[76]. These newly described molecular actions of these previously unappreciated families of lipid-derived mediators may shed light on the clinically recognized beneficial effects of omega-3 fatty acids. In addition to its role in controlling inflammation, EPA is the only omega-3 fatty acid shown to inhibit the aggrecanase enzymes responsible for cartilage degredation in dogs.[77-79] This inhibition occurs at the level of the mRNA, and is thought to be important in moderating the progression of cartilage degradation and thereby delaying disease progression.

The Challenge: Which Nutritional Recommendation; Osteoarthritis or Obesity?

Osteoarthritis is usually irreversible but as discussed nutritional management can minimize pain and slow the progression of the disease. It is generally accepted that the multimodal approach to managing dogs with OA must include weight management and nutritional joint support.[80] Hill's Prescription Diet j/d canine is an easy and effective means of providing nutritional joint support. In theory weight loss has a simple nutritional solution too. Simply provide fewer calories for consumption than the calories an individual needs to maintain a healthy weight. However prior to the introduction of the

Hill's Healthy Weight Protocol Tools and Prescription Diet® Metabolic Advanced Weight Solution communicating and implementing a weight management program could be a challenging endeavor for the veterinary health care team. Historically, one common cause for inconsistent results with weight management has been owner behaviors that are beyond the control of the veterinary health care team.[81] Even when owners try to follow appropriate recommendations and use manufacturer provided cups on average they tend to overestimate volumes by 10-20%.[82] Over the long term, these inaccuracies can predispose pets to weight gain and may be a significant factor in the failure of weight management programs using traditional therapeutic weight loss foods. Metabolic Advanced Weight Solution overcomes these obstacles. In a landmark in-home study, over 350 overweight or obese pets (159 dogs and 155 cats) completed a 2-month feeding study designed to document weight loss in real world conditions.[83] Remarkably, even without strict protocols and precise measuring, 88% of these pets lost weight at an average rate of 0.7% of initial body weight per week. The majority of pet owners agreed that Hill's® Prescription Diet® Metabolic Advanced Weight Solution was an easy way for their pet to lose weight, while keeping their pets feeling full and satisfied. This success may be due in part to Metabolic's positive impact on energy metabolism during weight loss and maintenance which results in reduced body fat and increased lean body mass in both dogs and cats.[84,85] By increasing energy metabolism during weight loss, Metabolic Advanced Weight Solution allows pets to successfully lose weight often in spite of their owners.

Given the documented benefits of Metabolic Advanced Weight Solution and j/d Canine, what is the best specific nutritional recommendation for overweight dogs with OA? Traditionally, in pets with multiple conditions, the veterinary health care team has been forced to decide which condition will benefit most from nutritional management. This can be challenging when strong evidence for nutritional management exists for both conditions. Efforts to incorporate both nutritional recommendations into a multimodal approach can lead to complicated instructions that owners may find onerous and ultimately unsuccessful.

One nutritional solution for two common conditions.

The introduction of Hill's Prescription Diet® Metabolic Plus Canine Mobility offers the veterinary health care team a new option with the power of 'and'. Metabolic Plus Moblity combines the benefits of two proven nutritional solutions; Metabolic Advanced Weight Solution and j/d Canine. Now you have one food with clinically proven nutrition

to manage obesity and osteoarthritis. Formulated with a synergistic blend of natural ingredients shown to activate metabolism and help dogs lose weight; and with high levels of omega-3 fatty acids to reduce inflammation and interrupt the degradation of cartilage Metabolic Plus Mobility is the one solution for overweight dogs with osteoarthritis. For canine patients it is now easier than ever before to customize a specific nutritional solution for the unique circumstances of each pet.

Arthritis with Normal BCS	Overweight	OA **AND** OW
j/d Canine	Metabolic Advanced Weight Solution	Metabolic Plus Mobility

Consequences of Abnormal Body Composition: Feline Lower Urinary Tract Disease and Obesity

Like dogs and humans the global incidence of overweight or obese cats has steadily increased in recent decades. Current estimates suggest that globally 30 -50% cats are overweight or obese.[7,8] Over the last five years, one US study documents that the number of overweight or obese cats has increased by an astonishing 90% which may reflect an increase in awareness as well as a true increase in the prevalence of overweight cats.[86] Obesity has been associated with a variety of conditions in cats including diabetes mellitus, hepatic lipidosis, dermatopathies, lameness, and urinary tract signs.[87,88] Diabetes mellitus is perhaps the condition most often associated with overweight cats, however, lower urinary tract signs may actually be more common. In fact, based on claims to VPI Pet Insurance, in 2013 feline lower urinary tract signs were the most common claim submission while diabetes was listed as the 6th most common.[89] According to pets.webmd.com about 10% of cats presented for veterinary care are diagnosed with lower urinary tract signs.[90] The combined results from three North American and one European study (n=23,235) of cats presenting with lower urinary tract signs (LUTS) indicate that feline idiopathic cystitis (FIC) is the most common cause (60%) followed by uroliths (20%) and urethral plugs (15%).[91-94]

COMMON CAUSES OF LUTS

Plugs
15%

Misc
5%

Uroliths
20%

FIC
60%
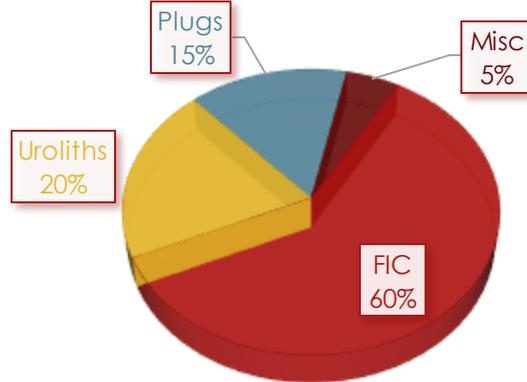
Excess weight is considered a risk factor for many of the conditions that cause lower urinary tract signs in humans and cats. While studies linking obesity and urolithiasis in cats have not been reported, there are reports finding associations of these two conditions in humans[25,26] The link is significant enough that human health care providers are encouraged to recommend both dietary modification and weight loss to obese patients to reduce the risk of kidney stone formation. The consistently reported increased risk of uroliths in neutered cats provides indirect evidence for the association between obesity and risk of urolithiasis.[95,96] Neutering is a well-recognized risk factor for obesity in cats.[97-103] Indoor housed cats are also at increased risk for lower urinary tract signs. Again, obesity is more common in cats housed indoors due to a more sedentary lifestyle. [102,104,105]

Obesity is also a risk factor for FIC, the most common cause of lower urinary tract signs. Results of a 2011 retrospective case controlled study documented that compared to controls cats with FIC had significantly lower activity levels (P < 0.001), exhibited less hunting behavior (P= 0.006) and had higher body condition scores (P = 0.008).[106] Interestingly these cats were also characterized as being significantly more nervous (P < 0.001) and fearful (P < 0.001) than other cats in the same household and were more prone to hide from unknown visitors in the house (P = 0.002). In fact, recent work suggests that FIC may be suffering from a systemic disease characterized by an abnormal response to stress which affects the lower urinary tract (LUT) rather than a disorder of the LUT.[107] Given the association between obesity and LUTS it is interesting to note that in humans, among other diseases, maladaptation to repeated or chronic stress stimuli plays a key role in increasing individual susceptibility to the development of obesity. Specific pathophysiological mechanisms may include hyper-activation of the hypothalamic-pituitary-adrenal (HPA) axis, which once activated may persist.[108] Recent

work in cats with FIC suggests altered HPA axis results in unrestrained sympathetic nervous system (SNS) which stimulates C-fibers and pain receptors of the bladder inciting a cascade of events including release of inflammatory mediators that result in the clinical manifestations which typify FIC.[109-112] While this mechanism has not been fully elucidated treatment plans for cats with FIC should include weight management as well as mechanisms to decrease stress and control inflammation.[113] As previously discussed, Metabolic Advanced Weight Solution is clinically proven to work with each pet's unique metabolic response to support healthy weight loss and maintenance. Importantly since it can be fed for both weight loss and weight maintenance, Metabolic is the perfect solution for multicat households.

## The Challenge: Which Nutritional Recommendation; LUTS or Obesity?
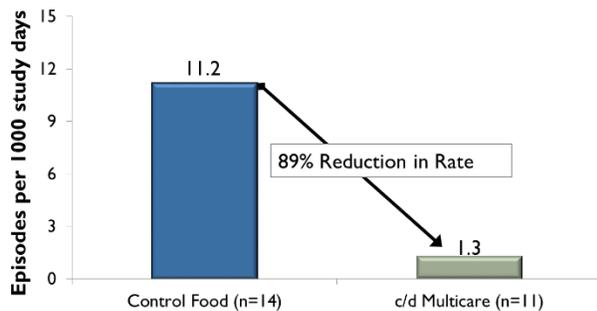
While weight loss is important for cats with LUTS, it is also important to manage the underlying condition. Studies confirm Hill's® Prescription Diet® c/d® Multicare Feline is the best choice for managing two of the most common causes of LUTS in cats; FIC and Struvite Urolithiasis. For cats with FIC a multimodal approach which includes environmental enrichment as well as dietary management is recommended.[114] The best currently available evidence is for dietary management with Hill's® Prescription Diet® c/d® Multicare Feline dry food.[115] In this year-long randomized controlled clinic study of cats with naturally occurring FIC cats consuming c/d Multicare dry food had significantly fewer episodes of FIC signs ($p < 0.05$) than cats eating a control food. Investigators concluded that consistent feeding of c/d Multicare to cats with FIC resulted in an 89% reduction in the rate of recurrent episodes of FIC signs. This is the first study to definitively demonstrate the impact of a food on the expression of FIC signs in cats.

For cats with struvite uroliths medical dissolution is generally the primary goal of therapy. Since first described in 1983 dietary dissolution of struvite uroliths has been recognized as safe and effective.[116-119] A recently publish study documents that struvite stones dissolved in as little as 7 days

Struvite Dissolution Times
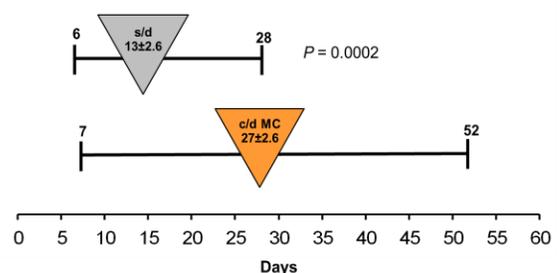
(mean 27 days) when cats were fed Hill's® Prescription Diet® c/d® Multicare Feline dry food.[119]

While medical dissolution of calcium oxalate uroliths, the second most common urolith in cats is not currently possible results of a recent study suggest nutritional management is important for reducing recurrence.[120] In this two year-long study of cats with naturally occurring calcium oxalate stones suggest that recurrence of calcium oxalate uroliths may be lower in cats fed the nutrition of Hill's® Prescription Diet® c/d® Multicare.

One nutritional solution for two common conditions.

The introduction of Hill's Prescription Diet® Metabolic Plus Urinary offers the veterinary health care team a new option with the power of 'and'. Metabolic Plus Urinary combines the benefits of two proven nutritional solutions; Metabolic Advanced Weight Solution and c/d Multicare. Now you have one food with clinically proven nutrition to manage obesity and common causes of LUTS. Formulated with a synergistic blend of natural ingredients shown to activate metabolism and help cats lose weight; and high levels of Omega-3 fatty acids (EPA and DHA) and antioxidants to help break the cycle of inflammation in patients with Feline Idiopathic Cystitis (FIC) Metabolic Plus Urinary is the one solution for overweight cats with lower urinary tract signs. For feline patients it is now easier than ever before to customize a specific nutritional solution for the unique circumstances of each pet.

LUTS with Normal BCS	Overweight	OA **AND** LUTS
c/d Multicare c/d Multicare Stress	Metabolic Advanced Weight Solution	Metabolic Plus Urinary

Summary: The Power of 'AND'

Perhaps Leonardo da Vinci said it best, "Simplicity is the ultimate sophistication". The introduction of Hill's Prescription Diet Metabolic Plus Mobility and Metabolic Plus Urinary provide pets, pet owners and the veterinary health care team with a sophisticated yet simple nutritional option for managing some of the most common concurrent conditions in veterinary medicine.

References

1.   Popkin BM. The World is Fat. *Scientific American,* 2007;88-95.
2.   Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet* 2014.
3.   Finucane MM, Stevens GA, Cowan MJ, et al. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet* 2011;377:557-567.
4.   Flegal KM, Kit BK, Orpana H, et al. Association of all-cause mortality with overweight and obesity using standard body mass index categories: a systematic review and meta-analysis. *JAMA* 2013;309:71-82.
5.   Sturm R. Increases in clinically severe obesity in the United States, 1986-2000. *Arch Intern Med* 2003;163:2146-2148.
6.   Sturm R, Hattori A. Morbid obesity rates continue to rise rapidly in the United States. *Int J Obes (Lond)* 2013;37:889-891.
7.   Bland IM, Hill J. Tackling dog obesity by tackling owner attitudes. *Perspectives in Agriculture, Veterinary Science, Nutrition and Natural Resources* 2011;6:1-7.
8.   McGreevy PD, Thomson PC, Pride C, et al. Prevalence of obesity in dogs examined by Australian veterinary practices and the risk factors involved. *Vet Rec* 2005;156:695-702.
9.   Klausner JS, Lund E. State of Pet Health 2012. Portland, OR: Banfield Pet Hospitals, 2012.
10.   Courcier EA, Thomson RM, Mellor DJ, et al. An epidemiological study of environmental factors associated with canine obesity. *J Small Anim Pract* 2010;51:362-367.
11.   Budsberg SC, Bartges JW. Nutrition and osteoarthritis in dogs: does it help? *Vet Clin North Am Small Anim Pract* 2006;36:1307-1323, vii.
12.   Lund EM, Armstrong PJ, Kirk CA, et al. Prevalence and Risk Factors for Obesity in Adult Dogs from Private US Veterinary Practices. *Intern J Appl Res Vet Med* 2006;4:177-186.
13.   White GA, Hobson-West P, Cobb K, et al. Canine obesity: is there a difference between veterinarian and owner perception? *J Small Anim Pract* 2011;52:622-626.
14.   Edney AT, Smith PM. Study of obesity in dogs visiting veterinary practices in the United Kingdom. *Vet Rec* 1986;118:391-396.
15.   Ward E, Budsberg S, Peterson M, et al. 2013 National Pet Obesity Awareness Day Survey Results: The Association for Pet Obesity Prevention (APOP), 2014.
16.   Kronfeld DS, Donoghue S, Glickman LT. Body condition of cats. *J Nutr* 1994;124:2683S-2684S.
17.   Witzel AL, Kirk CA, Henry GA, et al. Use of a morphometric method and body fat index system for estimation of body composition in overweight and obese cats. *J Am Vet Med Assoc* 2014;244:1285-1290.
18.   Witzel AL, Kirk CA, Henry GA, et al. Use of a novel morphometric method and body fat index system for estimation of body composition in overweight and obese dogs. *J Am Vet Med Assoc* 2014;244:1279-1284.
19.   Laflamme DP. Development and validation of a body condition score system for cats: A clinical tool. *Feline Practice* 1997;25:13-18.
20.   Laflamme DP. Development and validation of a body condition score system for dogs: A clinical tool. *Canine Practice* 1997;22:10-15.
21.   Thatcher C, Hand M, Remillard R. Small animal clinical nutrition: an iterative process In: Hand MS, Thatcher CD, Remillard RL, et al., eds. *Small Animal Clinical Nutrition 5th Edition*. Topeka, KS: Mark Morris Institute, 2010;3-21.
22.   Gregor MF, Hotamisligil GS. Inflammatory mechanisms in obesity. *Annu Rev Immunol* 2011;29:415-445.
23.   Savini I, Catani MV, Evangelista D, et al. Obesity-associated oxidative stress: strategies finalized to improve redox state. *Int J Mol Sci* 2013;14:10497-10538.
24.   Suresh S, Mahendra J. Multifactorial relationship of obesity and periodontal disease. *J Clin Diagn Res* 2014;8:ZE01-03.
25.   Taylor EN, Stampfer MJ, Curhan GC. Obesity, weight gain, and the risk of kidney stones. *JAMA* 2005;293:455-462.
26.   Semins MJ, Shore AD, Makary MA, et al. The association of increasing body mass index and kidney stone disease. *J Urol* 2010;183:571-575.
27.   Chandra A, Biersmith M, Tolouian R. Obesity and kidney protection. *J Nephropathol* 2014;3:91-97.
28.   Laflamme DP. Understanding and managing obesity in dogs and cats. *Vet Clin North Am Small Anim Pract* 2006;36:1283-1295, vii.
29.   Kealy RD, Lawler DF, Ballam JM, et al. Effects of diet restriction on life span and age-related changes in dogs. *J Am Vet Med Assoc* 2002;220:1315-1320.
30.   Griffon DJ. A review of the pathogenesis of canine cranial cruciate ligament disease as a basis for future preventive strategies. *Vet Surg* 2010;39:399-409.

31.   Marshall W, Bockstahler B, Hulse D, et al. A review of osteoarthritis and obesity: current understanding of the relationship and benefit of obesity treatment and prevention in the dog. *Vet Comp Orthop Traumatol* 2009;22:339-345.

32.   Brady RB, Sidiropoulos AN, Bennett HJ, et al. Evaluation of gait-related variables in lean and obese dogs at a trot. *Am J Vet Res* 2013;74:757-762.

33.   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.

34.   Yamka RM, Friesen KG, Lowry S, et al. Measurement of Arthritic and Bone Serum Metabolites in Arthritic, Non-Arthritic, and Geriatric Cats Fed Wellness Foods. *International Journal of Applied Research in Veterinary Medicine* 2006;4:265-273.

35.   Smith GK, Popovitch CA, Gregor TP, et al. Evaluation of risk factors for degenerative joint disease associated with hip dysplasia in dogs. *J Am Vet Med Assoc* 1995;206:642-647.

36.   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.

37.   Runge JJ, Kelly SP, Gregor TP, et al. Distraction index as a risk factor for osteoarthritis associated with hip dysplasia in four large dog breeds. *J Small Anim Pract* 2010;51:264-269.

38.   Krontveit RI, Trangerud C, Saevik BK, et al. Risk factors for hip-related clinical signs in a prospective cohort study of four large dog breeds in Norway. *Prev Vet Med* 2012;103:219-227.

39.   van Hagen MA, Ducro BJ, van den Broek J, et al. Incidence, risk factors, and heritability estimates of hind limb lameness caused by hip dysplasia in a birth cohort of boxers. *Am J Vet Res* 2005;66:307-312.

40.   Powers MY, Martinez SA, Lincoln JD, et al. Prevalence of cranial cruciate ligament rupture in a population of dogs with lameness previously attributed to hip dysplasia: 369 cases (1994-2003). *J Am Vet Med Assoc* 2005;227:1109-1111.

41.   Witsberger TH, Villamil JA, Schultz LG, et al. Prevalence of and risk factors for hip dysplasia and cranial cruciate ligament deficiency in dogs. *J Am Vet Med Assoc* 2008;232:1818-1824.

42.   Whitehair JG, Vasseur PB, Willits NH. Epidemiology of cranial cruciate ligament rupture in dogs. *J Am Vet Med Assoc* 1993;203:1016-1019.

43.   Grierson J, Asher L, Grainger K. An investigation into risk factors for bilateral canine cruciate ligament rupture. *Vet Comp Orthop Traumatol* 2011;24:192-196.

44.   Klausner JS, Lund E. State of Pet Health 2013. Portland, OR: Banfield Pet Hospitals, 2013.

45.   DG ON, Church DB, McGreevy PD, et al. Prevalence of disorders recorded in dogs attending primary-care veterinary practices in England. *PLoS One* 2014;9:e90501.

46.   Klausner JS, Lund E. State of Pet Health 2014. Portland, OR: Banfield Pet Hospitals, 2014.

47.   Klausner JS, Lund E. State of Pet Health 2011 Portland, OR: Banfield Pet Hospitals, 2011.

48.   Lavrijsen IC, Heuven HC, Meij BP, et al. Prevalence and co-occurrence of hip dysplasia and elbow dysplasia in Dutch pure-bred dogs. *Prev Vet Med* 2014;114:114-122.

49.   Genevois JP, Remy D, Viguier E, et al. Prevalence of hip dysplasia according to official radiographic screening, among 31 breeds of dogs in France. *Vet Comp Orthop Traumatol* 2008;21:21-24.

50.   Yusuf E, Nelissen RG, Ioan-Facsinay A, et al. Association between weight or body mass index and hand osteoarthritis: a systematic review. *Ann Rheum Dis* 2010;69:761-765.

51.   Teichtahl AJ, Wang Y, Wluka AE, et al. Obesity and knee osteoarthritis: new insights provided by body composition studies. *Obesity (Silver Spring)* 2008;16:232-240.

52.   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.

53.   Trayhurn P, Wood IS. Adipokines: inflammation and the pleiotropic role of white adipose tissue. *Br J Nutr* 2004;92:347-355.

54.   Burkholder WJ, Taylor L, Hulse DA. Weight loss to optimal body condition increases ground reactive forces in dogs with osteoarthritis. Purina Nutrition Forum 2000;74.

55.   Impellizeri JA, Tetrick MA, Muir P. Effect of weight reduction on clinical signs of lameness in dogs with hip osteoarthritis. *J Am Vet Med Assoc* 2000;216:1089-1091.

56.   Woolf AD, Breedveld F, Kvien TK. Controlling the obesity epidemic is important for maintaining musculoskeletal health. *Ann Rheum Dis* 2006;65:1401-1402.

57.   Rosales Ade L, Brito NL, Frucchi R, et al. Obesity, ostearthritis and clinical treatment. *Acta Ortop Bras* 2014;22:136-139.

58.   Garver MJ, Focht BC, Dials J, et al. Weight status and differences in mobility performance, pain symptoms, and physical activity in older, knee osteoarthritis patients. *Arthritis* 2014;2014:375909.

59.   Schoffman DE, Wilcox S, Baruth M. Association of body mass index with physical function and health-related quality of life in adults with arthritis. *Arthritis* 2013;2013:190868.

60.   Gudbergsen H, Boesen M, Lohmander LS, et al. Weight loss is effective for symptomatic relief in obese subjects with knee osteoarthritis independently of joint damage severity assessed by high-field MRI and radiography. *Osteoarthritis Cartilage* 2012;20:495-502.

61.   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.

62.   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.

63.	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.

64.	Kealy RD, Lawler DF, Ballam JM, et al. Ev aluation of the effect of limited food consumption on radiographic evidence of osteoarthritis in dogs. *J Am Vet Med Assoc* 2000;217:1678-1680.

65.	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.

66.	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.

67.	Mlacnik E, Bockstahler BA, Muller M, et al. Effects of caloric restriction and a moderate or intense physiotherapy program for treatment of lameness in ov erweight dogs with osteoarthritis. *J Am Vet Med Assoc* 2006;229:1756-1760.

68.	Kirkby KA, Lewis DD. Canine hip dysplasia: reviewing the evidence for nonsurgical management. *Vet Surg* 2012;41:2-9.

69.	Vandeweerd JM, Coisnon C, Clegg P, et al. Systematic rev iew of efficacy of nutraceuticals to allev iate clinical signs of osteoarthritis. *J Vet Intern Med* 2012;26:448-456.

70.	Roush JK, Cross AR, Renberg WC, et al. Ev aluation of the effects of dietary supplementation with fish oil omega-3 fatty acids on weight bearing in dogs with osteoarthritis. *J Am Vet Med Assoc* 2010;236:67-73.

71.	Fritsch DA, Allen TA, Dodd CE, et al. A multicenter study of the effect of dietary supplementation with fish oil omega-3 fatty acids on carprofen dosage in dogs with osteoarthritis. *J Am Vet Med Assoc* 2010;236:535-539.

72.	Fritsch D, Allen TA, Dodd CE, et al. Dose-titration effects of fish oil in osteoarthritic dogs. *J Vet Intern Med* 2010;24:1020-1026.

73.	Roush JK, Dodd CE, Fritsch DA, et al. Multicenter veterinary practice assessment of the effects of omega-3 fatty acids on osteoarthritis in dogs. *J Am Vet Med Assoc* 2010;236:59-66.

74.	Caterson B, Flannery CR, Hughes CE, et al. Mechanisms involved in cartilage proteoglycan catabolism. *Matrix Biology* 2000;19:333-344.

75.	Serhan CN. Nov el omega -- 3-derived local mediators in anti-inflammation and resolution. *Pharmacology and Therapeutics* 2005;105:7-21.

76.	Schwab JM, Serhan CN. Lipoxins and new lipid mediators in the resolution of inflammation. *Current Opinion in Pharmacology* 2006;6:414-420.

77.	Caterson B, Flannery CR, Hughes CE, et al. Mechanisms involved in cartilage proteoglycan catabolism. *Matrix Biol* 2000;19:333-344.

78.	Innes JF, Little CB, Hughes CE, et al. Products resulting from cleav age of the interglobular domain of aggrecan in samples of synov ial fluid collected from dogs with early- and late-stage osteoarthritis. *Am J Vet Res* 2005;66:1679-1685.

79.	Arner EC, Hughes CE, Decicco CP, et al. Cytokine-induced cartilage proteoglycan degradation is mediated by aggrecanase. *Osteoarthritis Cartilage* 1998;6:214-228.

80.	Rychel JK. Diagnosis and treatment of osteoarthritis. *Top Companion Anim Med* 2010;25:20-25.

81.	Bland IM, Guthrie-Jones A, Taylor RD, et al. Dog obesity: v eterinary practices' and owners' opinions on cause and management. *Prev Vet Med* 2010;94:310-315.

82.	German AJ, Holden SL, Mason SL, et al. Imprecision when using measuring cups to weigh out extruded dry kibbled food. *J Anim Physiol Anim Nutr (Berl)* 2011;95:368-373.

83.	In home weight loss study in dogs and cats. Hill's Pet Nutrition, Inc. Data on file, 2012.

84.	Jewell DE, Floerchinger AM, Jackson M, et al. A reduced calorie, high fiber food with added coconut oil, L-carnitine, lysine and leucine increases basal metabolic rate in overweight and obese cats (Abstract). *Journal of Veterinary Internal Medicine* 2014;28:1088.

85.	Jewell DE, Floerchinger AM, Jackson M, et al. A reduced calorie, high fiber food with added coconut oil, L-carnitine, lysine and leucine increases basal metabolic rate in overweight and obese dogs (Abstract). *Journal of Veterinary Internal Medicine* 2014;28:1087-1088.

86.	Klausner JS, Lund E. Banfield Pet Hospital State of Pet Health 2012, 2012.

87.	Scarlett JM, Donoghue S. Associations between body condition and disease in cats. *J Am Vet Med Assoc* 1998;212:1725-1731.

88.	Lund EM, Armstrong PJ, Kirk C, et al. Prev alence and risk factors for obesity in adult cats from priv ate US v eterinary practices. *Intern J Appl Res Vet Med* 2005;3:88-96.

89.	Insurance VP. Top 10 Reasons Pets Visit Vets, 2013.

90.	Martinez E. 6 Most Common Cat Health Problems. WebMD Veterinary Reference, 2014.

91.	Kruger JM, Osborne CA, Goyal SM, et al. Clinical ev aluation of cats with lower urinary tract disease. *J Am Vet Med Assoc* 1991;199:211-216.

92.	Buffington CA, Chew DJ, Kendall MS, et al. Clinical ev aluation of cats with nonobstructive urinary tract diseases. *J Am Vet Med Assoc* 1997;210:46-50.

93.	Lekcharosensuk C, Osborne CA, Lulich JP. Epidemiologic study of risk factors for lower urinary tract diseases in cats. *J Am Vet Med Assoc* 2001;218:1429-1435.

94.	Gerber B, Boretti FS, Kley S, et al. Ev aluation of clinical signs and causes of lower urinary tract disease in European cats. *J Small Anim Pract* 2005;46:571-577.

95.	Appel SL, Houston DM, Moore AE, et al. Feline urate urolithiasis. *Can Vet J* 2010;51:493-496.

96.	Lekcharoensuk C, Lulich JP, Osborne CA, et al. Association between patient-related factors and risk of calcium oxalate and magnesium ammonium phosphate urolithiasis in cats. *J Am Vet Med Assoc* 2000;217:520-525.

97.   Alexander LG, Salt C, Thomas G, et al. Effects of neutering on food intake, body weight and body composition in growing female kittens. *Br J Nutr* 2011;106 Suppl 1:S19-23.

98.   Backus RC, Cave NJ, Keisler DH. Gonadectomy and high dietary fat but not high dietary carbohydrate induce gains in body weight and fat of domestic cats. *Br J Nutr* 2007;98:641-650.

99.   Corbee RJ. Obesity in show cats. *J Anim Physiol Anim Nutr (Berl)* 2014.

100.   Courcier EA, Mellor DJ, Pendlebury E, et al. An investigation into the epidemiology of feline obesity in Great Britain: results of a cross-sectional study of 47 companion animal practises. *Vet Rec* 2012;171:560.

101.   Colliard L, Paragon BM, Lemuet B, et al. Prevalence and risk factors of obesity in an urban population of healthy cats. *J Feline Med Surg* 2009;11:135-140.

102.   Scarlett JM, Donoghue S, Saidla J, et al. Overweight cats: prevalence and risk factors. *Int J Obes Relat Metab Disord* 1994;18 Suppl 1:S22-28.

103.   Kienzle E, Moik K. A pilot study of the body weight of pure-bred client-owned adult cats. *Br J Nutr* 2011;106 Suppl 1:S113-115.

104.   Kienzle E, Bergler R. Human-animal relationship of owners of normal and overweight cats. *J Nutr* 2006;136:1947S-1950S.

105.   Allan FJ, Pfeiffer DU, Jones BR, et al. A cross-sectional study of risk factors for obesity in cats in New Zealand. *Prev Vet Med* 2000;46:183-196.

106.   Defauw PA, Van de Maele I, Duchateau L, et al. Risk factors and clinical presentation of cats with feline idiopathic cystitis. *J Feline Med Surg* 2011;13:967-975.

107.   Buffington CA. Idiopathic cystitis in domestic cats--beyond the lower urinary tract. *J Vet Intern Med* 2011;25:784-796.

108.   Pasquali R. The hypothalamic-pituitary-adrenal axis and sex hormones in chronic stress and obesity: pathophysiological and clinical aspects. *Ann N Y Acad Sci* 2012;1264:20-35.

109.   Westropp JL, Kass PH, Buffington CA. Evaluation of the effects of stress in cats with idiopathic cystitis. *Am J Vet Res* 2006;67:731-736.

110.   Westropp JL, Kass PH, Buffington CA. In vivo evaluation of alpha(2)-adrenoceptors in cats with idiopathic cystitis. *Am J Vet Res* 2007;68:203-207.

111.   Wu CH, Buffington CA, Fraser MO, et al. Urodynamic evaluation of female cats with idiopathic cystitis. *Am J Vet Res* 2011;72:578-582.

112.   Lavelle JP, Meyers SA, Ruiz WG, et al. Urothelial pathophysiological changes in feline interstitial cystitis: a human model. *Am J Physiol Renal Physiol* 2000;278:F540-553.

113.   Kerr KR. Companion Animals Symposium: dietary management of feline lower urinary tract symptoms. *J Anim Sci* 2013;91:2965-2975.

114.   Buffington CA, Westropp JL, Chew DJ, 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.

115.   Kruger JM, Lulich J, Merrills J, et al. A Year-Long Prospective, Randomized, Double-Masked study of Nutrition on Feline Idiopathic Cystitis. Proceedings American College of Veterinary Internal Medicine Annual Forum 2013.

116.   Osborne CA, Lulich JP, Kruger JM, et al. Medical dissolution of feline struvite urocystoliths. *J Am Vet Med Assoc* 1990;196:1053-1063.

117.   Houston DM, Rinkardt NE, Hilton J. Evaluation of the efficacy of a commercial diet in the dissolution of feline struvite bladder uroliths. *Vet Ther* 2004;5:187-201.

118.   Houston DM, Weese HE, Evason MD, et al. A diet with a struvite relative supersaturation less than 1 is effective in dissolving struvite stones in vivo. *Br J Nutr* 2011;106 Suppl 1:S90-92.

119.   Lulich JP, Kruger JM, Macleay JM, et al. Efficacy of two commercially available, low-magnesium, urine-acidifying dry foods for the dissolution of struvite uroliths in cats. *J Am Vet Med Assoc* 2013;243:1147-1153.

120.   Lulich J, Kruger JM, MacLeay J, et al. A two year long prospective, randomized, double-masked study of nutrition on the recurrence of calcium oxalate urolithiasis in stone forming cats. ACVIM Annual Forum 2014.