The Role of Nutritional Interventions in the Longevity and Maintenance of Long-Term Health in Aging Cats

Carolyn J. Cupp, DVM, MS[1]
Wendell W. Kerr, MS[2]
Clementine Jean-Philippe, DVM, PhD[3]
Avinash R. Patil, BVSc, PhD[2]
Gerardo Perez-Camargo, PhD, MRCVS[2]

[1]*Nestlé Purina PetCare Research*
St. Joseph, Missouri
[2]*Nestlé Purina PetCare Research*
St. Louis, Missouri
[3]*Nestlé Purina R&D Centre, Amiens*
Aubigny, France

KEY WORDS: aging, feline, nutrition, longevity, antioxidants

ABSTRACT

Ninety cats were assigned to a study to determine the effects of a blend of nutritional supplements including antioxidants, a prebiotic, and a blend of omega-3 and omega-6 fatty acids on longevity and quality of life in senior cats. Cats between the ages of 7 and 17 years were blocked to 1 of 3 groups by age, body condition, and gender and fed their assigned diets for their remaining lifetime. On average, cats eating the diet containing the nutritional blend lived significantly longer and showed significantly slower deterioration in a number of clinical health parameters compared to cats fed a standard adult maintenance control diet. Hematological measurements, body weight, lean body mass, skin thickness, and activity levels also were correlated to survival. Nutritional enhancements to the diet of senior cats can improve both length and quality of life.

INTRODUCTION

Extending the length of life while minimizing or delaying the onset of chronic disease and enhancing the quality of life in aging individuals is a goal common to both human and veterinary medicine. The role of nutrition in the modulation of health and disease has been studied extensively. Numerous veterinary diets have been developed to address specific clinical problems such as renal disease,[1,2] cardiac disease,[3] diabetes,[4] and inflammatory bowel disease,[5] but diets proven to extend healthy life in cats are lacking. Dietary modifications designed to compensate for declining functional systems during aging have the potential to improve both the quality and length of life of senior pets.

While many genetic and environmental factors play a role in the rate an individual may age, increased oxidative stress is generally thought to contribute to many age-related diseases.[6,7] Thus, supplementation of antioxidants in diets designed for senior pets would likely be of benefit. Additionally, continuing advances in human and pet nutri-

tion and increasing evidence for potential synergies among other types of functional foods and dietary supplements could mean added benefits for nutritional "cocktails" in these older pets.[8-11]

Initial results from a study to evaluate whether antioxidants, alone or in combination with other nutritional supplements, increased longevity in older cats showed that senior cats fed the supplemented diet lived significantly longer than cats fed a control diet and had other positive indicators of improved health.[12] The study tested the hypothesis that combining antioxidants with supplemental polyunsaturated fatty acids and a prebiotic fiber could measurably benefit the health and longevity of aging cats.

The objective of this report is to review the first 7 years of longevity data from this same study and present data on some additional health parameters (hematology, serum glucose, skin fold thickness, and activity levels) that have been measured over that time period.

MATERIALS AND METHODS

Study Design

A multi-year feeding study was initiated in February 2000 with 90 healthy mixed-breed cats, ranging in age from 7 to 17 years. Cats were divided into 3 chronological age groups of 30 cats each: 7 to 9 years, 10 to 12 years, and 13 or more years. Groups were stratified to ensure a balance of age, gender, and body condition, prior to randomly assigning groups to dietary treatment. Cats were housed individually or in groups, according to their accustomed housing, and housing was similar across groups. Food was provided ad libitum with the exception of an overnight fast prior to anesthesia or blood collection. Water was available at all times. The study protocol was reviewed and approved by the Nestlé Purina Product Technology Center (PTC, St. Joseph, Missouri, USA) Animal Care and Use Committee.

Cats were assigned to 1 of 3 isocaloric diets: Diet 1 (control): nutritionally complete and balanced adult cat food; Diet 2: control formula + antioxidants (vitamin E as alpha tocopheryl acetate and beta carotene); and Diet 3: control formula + antioxidants + prebiotic (whole chicory root) + blend of oils (supplemental source of omega-6 and omega-3 fatty acids). Diets were produced every 6 to 8 weeks in the Nestlé Purina PTC. Typical nutrient comparisons were previously reported.[12] The test diets were fed as the exclusive source of nutrition, except for water, for the remaining lifetime of each cat assigned to the trial. If a cat refused to eat the test diet and medical work-up revealed no health-related conditions, the cat was considered for removal from the study after all avenues to improve consumption short of a change in diet were attempted.

Cats were pre-screened prior to being assigned to the study to ensure good health. Health monitoring and treatment of all animals were carried out according to established colony veterinary procedures and recorded in the individual health records. Veterinary personnel were blinded to dietary treatment groups, and diets were not adjusted due to illness. Humane euthanasia was carried out according to established colony procedures only after all appropriate diagnostic procedures, therapeutic regimens, and multiple assessments failed to show a clinical response, and the staff veterinarian deemed the cat's prognosis poor.

Data Collection

The following measurements were taken for all cats at study initiation and at regular intervals throughout the study: complete physical examination, body condition score (BCS), bone density and body composition by dual-energy X-ray absorptiometry (DEXA), hematology, serum chemistry, serum thyroid hormone concentrations, plasma fatty acids, serum antioxidant status, fecal microflora, and complete urinalysis. Details for these procedures were previously described.[12] Food consumption was measured daily during the study, and body weights were assessed weekly. Clinical illnesses and treatments were recorded as they occurred, and post-mortem examinations

were conducted on all deceased cats, with tissues submitted for histopathology. Skin fold thickness was evaluated every 6 months using Mitutoyo® digital calipers (Mitutoyo America Corp., Aurora, IL, USA). Activity was measured for a continuous 48-hour period every 3 to 6 months on a subset of 48 cats (16 cats from each diet, randomly assigned and blocked by age, gender, and body condition) using Actiwatch® (Mini Mitter Co., Bend, OR, USA).

Routine veterinary dental prophylaxis was performed every 6 months, when cats were anesthetized for DEXA scanning. Anesthesia was performed according to established colony veterinary procedures, based on the health status of the cat.

Statistical Analysis

Analysis of variance was used to compare initial parameters across groups to confirm that randomization was effective in producing balance at baseline (t_0) in the 3 study groups, as previously reported.[12]

Survival analyses were performed to compare the 3 diets for the age at which the cats died (age at death) and the number of days the cats survived on the trial (days on trial). For age at death, an accelerated failure time (AFT) model assuming a normal distribution, also known as a censored regression, was performed.[13] For days on trial, a Cox's proportional hazard model was used to compare the survival rates of the 3 diets (pairwise comparison).[14] Hazard ratios along with their 95% confidence intervals were estimated. Both analyses were performed with the age the cats started on trial (initial age) as a covariate.

Analysis of measured health parameters was performed by a longitudinal analysis.[15] The longitudinal model allowed for each animal's trend to be considered over time and an average trend or slope predicted for each group. Where appropriate, a quadratic effect was included in the longitudinal model. For serum Vitamin E, the data did not show a linear change over time; therefore, repeated measures analysis of covariance was performed.

To determine if any of the measured parameters were related to survival, 2 types of analyses were performed. The first was a Cox's proportional hazard model using the measured parameter as a time-varying covariate. The Cox's model evaluates whether the parameter measured at a given time is related to the hazard at that time. The second analysis was a joint modeling of the longitudinal and survival models.[16] The joint modeling examines if there is a relationship between the survival of the animal and the slope and intercept from the longitudinal model; that is, are linear changes in the measured parameter related to survival.

All statistical calculations were performed using SAS.[17]

RESULTS

Study Population

A total of 15 cats were removed from the study for refusal to eat for non-health-related reasons. Ten of these were removed within the first 6 weeks of the trial and were replaced with other cats of similar age and gender to continue the study. Data analyses, including baseline values, represent the groups with the replacement cats. Five of the 15 cats were removed later in the study and were not replaced; 3 of those cats (1 from each dietary treatment group) were removed by the veterinarian more than 6 months after trial initiation. These 3 cats have been included in the statistical data set and are considered "censored" data, along with the remaining cats that are still living.

Baseline Data (t_0)

There were no significant differences in baseline clinical measures (age, weight), body composition (BCS, DEXA), hematological, or serum biochemical values between the 3 groups, indicating effective stratification of the 3 study groups.[12]

Longevity

For the survival analysis, there were 88 cats in the data set after 7.5 years: 81 had died, 3 were removed early as previously described, and 4 had not yet died at the time of

Table 1. Survival analysis (days on trial).

Variable	df	*P* Value	Hazard Ratio	95% CI for Hazard Ratio
Diet 1 vs Diet 2	1	0.2573	0.720	0.407-1.271
Diet 1 vs Diet 3	1	0.0054	0.424	0.231-0.776
Diet 2 vs Diet 3	1	0.2727	0.741	0.434-1.266

Table 2. Age at death (censored regression).

Diet	Predicted Age at Death	*P* Value	
1	14.29	Diet 1 vs Diet 2	0.7556
2	14.42	Diet 1 vs Diet 3	0.0129
3	15.23	Diet 2 vs Diet 3	0.0451

analysis. Survival analyses were performed to compare the 3 diets for days on trial and age at death.

The Cox's proportional hazard regression analysis using initial age as a covariate showed a significant difference for days on trial between Diets 1 and 3. The hazard ratio of Diet 1 versus Diet 3 was 0.424 ($P < 0.01$), meaning that the hazard of dying for the cats on Diet 3 was only 42% of the hazard of dying for the cats on Diet 1 (Table 1). There were no significant differences between Diets 1 and 2 or between Diets 2 and 3.

Comparison of the diets for age at death using censored regression analysis (AFT) and initial age as a covariate showed significant differences between Diets 1 and 3 ($P < 0.05$; Table 2), with cats on Diet 3 living about 1 year longer than cats on Diet 1.

Thus, 2 different methods for evaluating survival, days on trial and age at death, showed significant differences between Diets 1 and 3. Using age at death provides a specific quantitative measure, showing that cats on Diet 3 lived, on average, about a year longer than cats on Diet 1.

Blood

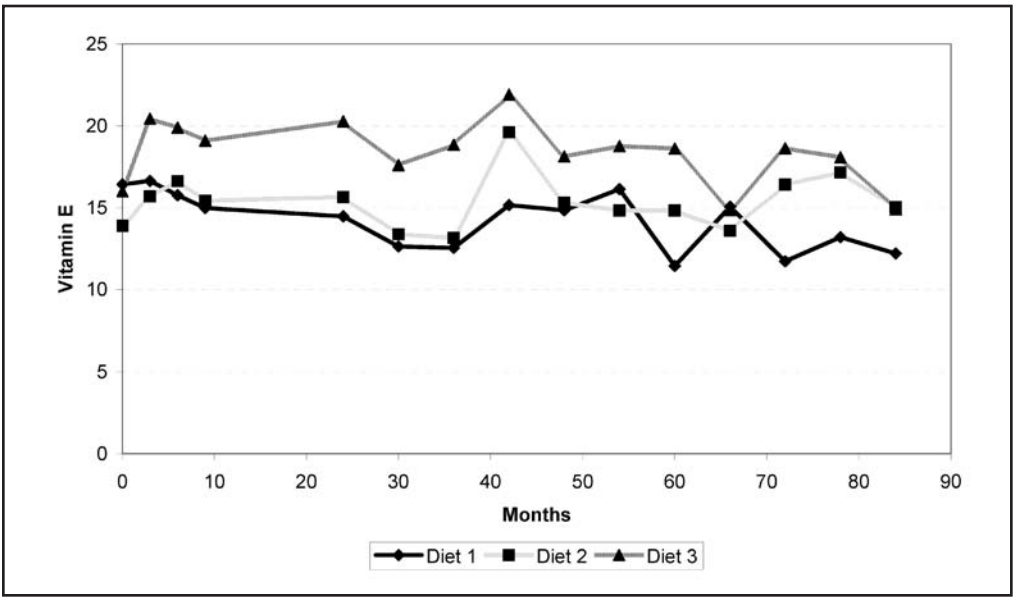
Serum vitamin E levels were evaluated at 0 (t0), 3, 6, 9, and 24 months, then every 6 months for the duration of the study. For the repeated measures analysis of covariance, initial age of the cats was the covariate in the model because of the wide range of starting ages of the cats. Examination of the least square means shows that at t_0, there was not a significant difference between the diets, while for times 3 through 42 months, Diet 3 averaged significantly higher than Diets 1 and 2 (Figure 1). While absolute levels of serum vitamin E held relatively steady throughout the trial for the cats on the 3 diets, statistical significance between the diets did not remain consistent after 42 months due to decreasing number of cats and loss of statistical power.

Survival analysis with vitamin E as a time-varying covariate was performed using a Cox's proportional hazard model. Modeling to relate vitamin E and other parameters to survival only included Diets 1 and 3 because they were the only diets that showed significant differences in survival. There was a significant relationship between survival and serum vitamin E ($P < 0.05$; Table 3). The hazard ratio of less than 1 suggests that increasing serum vitamin E decreases the hazard of dying.

Hematology and serum chemistry analyses, and measurements of skin fold thickness were performed at trial initiation and every 6 months for the duration of the study. For red blood cell (RBC) count, hematocrit (HCT), hemoglobin (HGB), and fasting glucose (GLU), a longitudinal analysis relating the parameter to time by diet showed significant or near significant differences (Figures 2, 3, and 4). Therefore, a series of analyses were done to relate change in the parameter over time with survival.

For RBC count, levels decreased over time for all diets, but the slopes for Diets 1 and 3 were significantly different ($P < 0.05$; Table 4), with cats eating Diet 1 showing a larger decrease over time than cats eating Diet 3. The Cox's proportional hazard model

Figure 1. Vitamin E LS means (initial age = 7 years).



with RBC count as a time-varying covariate showed a significant relationship between survival and RBC count (Table 3). Red blood cell count was positively correlated with survival, and the hazard ratio was less than 1, indicating that higher RBC count was associated with a decreased hazard of dying ($P < 0.05$). Joint modeling of the longitudinal and survival analysis also showed a significant relationship between both the intercept and slope from the longitudinal model and survival (Table 5), again showing that a higher RBC count was associated with longer survival.

For HCT, the longitudinal analysis showed that the slopes for Diets 1 and 3 were significantly different ($P < 0.05$; Table 4), with cats eating Diet 1 showing a significant decrease over time while cats on Diet 3 showed no change. The Cox's proportional hazard model with HCT as a time-varying covariate showed a significant relationship between survival and HCT (Table 3). Hematocrit was positively correlated with survival, and the hazard ratio was less than 1, indicating that higher HCT was associated with a decreased hazard of dying ($P < 0.05$). The joint longitudinal and survival analysis also showed that higher levels are associated with increased survival (Table 5).

For HGB, the longitudinal analysis showed that levels decreased over time for cats on all diets, and, while not significant, the slope for Diet 1 tended to decrease more than for Diet 3 ($P < 0.10$; Table 4). The Cox's proportional hazard model with HGB as a time-varying covariate showed a significant relationship between survival and HGB (Table 3). Hemoglobin was positively correlated with survival, and the hazard ratio was less than 1, indicating that higher HGB was associated with a decreased hazard of dying ($P < 0.05$). The joint longitudinal and survival analysis also showed that higher levels are associated with increased survival (Table 5).

Longitudinal analysis of serum glucose showed no significant differences by diet over time, but an indication of a trend for increased serum glucose for Diet 1 was observed ($P < 0.10$; Table 4). However, modeling using serum glucose with the survival variables showed no significant relationship between serum glucose and survival (Table 5).

Body Weight and Lean Body Mass

Body weight decreased over time for all groups, but to a lesser extent for cats on

Figure 2. Red blood cell predicted means (initial age = 7 years).

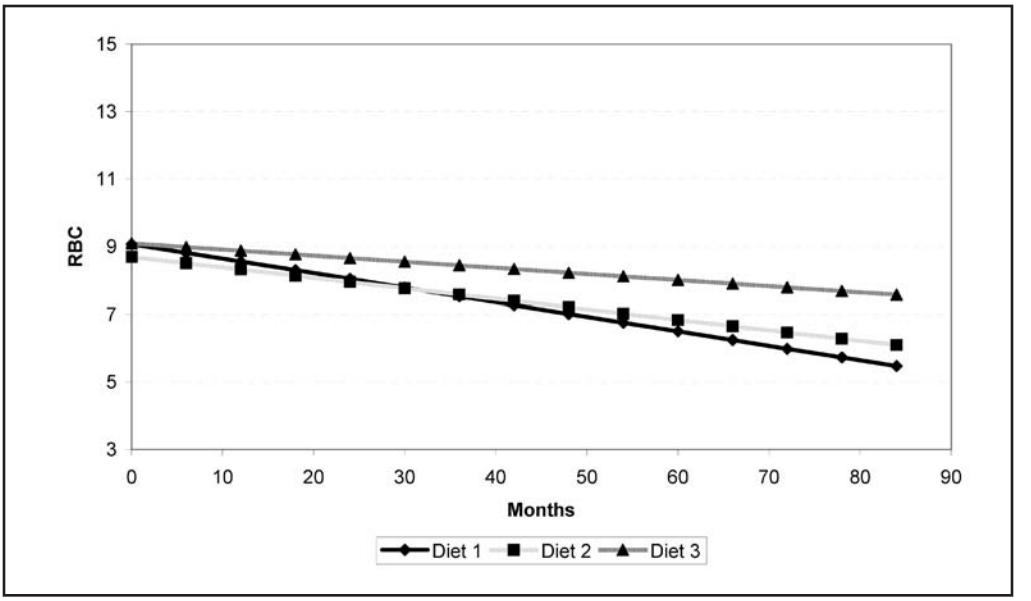
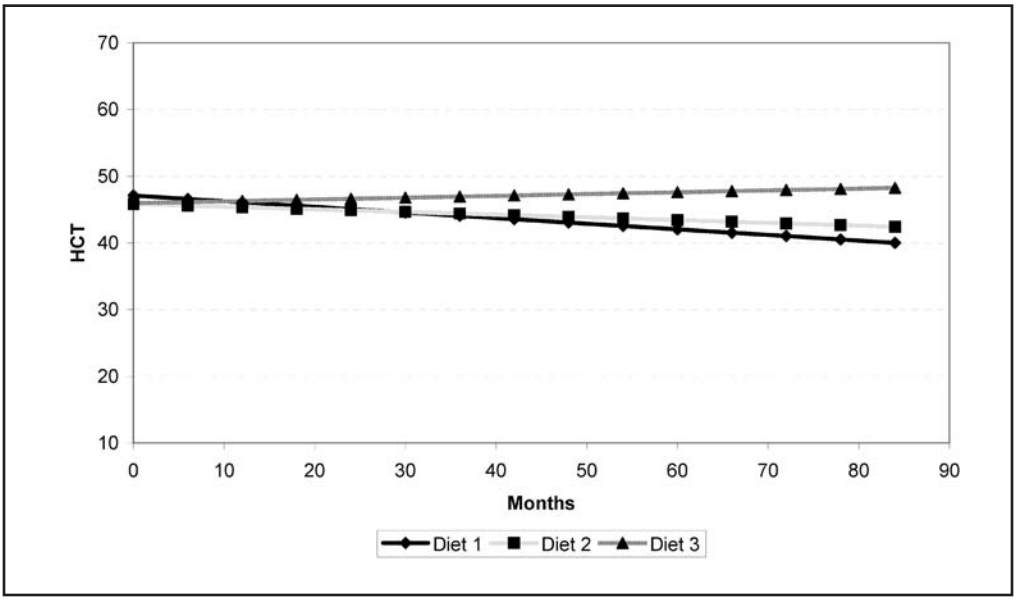


Figure 3. Hematocrit predicted means (initial age = 7 years).



Diet 3, as previously reported.[12] The Cox's proportional hazard model with body weight as a time-varying covariate showed a significant relationship between body weight and survival (Table 3). Body weight was positively correlated with survival, and the hazard ratio was less than 1, indicating that higher body weight was associated with a decreased hazard of dying ($P < 0.05$). The joint longitudinal and survival analysis also showed a significant relationship between both the intercept and slope from the longitudinal model and survival (Table 5), again showing that a higher body weight is associated with longer survival.

Longitudinal analysis of lean body mass (LBM) showed significant dietary differences in the average trend lines (Figure 5), with LBM of cats on Diet 3 decreasing less over time compared with either of the

Table 3. Survival analysis with time varying covariate, Diet 1 vs Diet 3.

Parameter	Hazard Ratio	*P* Value
Vitamin E	0.934	0.0127
Red blood cell count	0.588	<0.0001
Hematocrit	0.9	<0.0001
Hemoglobin	0.692	<0.0001
Glucose	1.003	0.6432
Body weight	0.333	<0.0001
Lean body mass	0.189	<0.0001
Skin thickness	0.144	<0.0001
Minutes active/day	0.873	0.0486

other 2 diets ($P < 0.05$; Table 4). The Cox's proportional hazard model with LBM as a time-varying covariate showed a significant relationship between survival and LBM (Table 3). Lean body mass was positively correlated with survival, and the hazard ratio was less than 1, indicating that higher LBM was associated with a decreased hazard of dying ($P < 0.05$). The joint longitudinal and survival analysis showed a significant relationship between the slopes from the longitudinal model and survival (Table 5), again showing that a higher LBM is associated with longer survival.

Skin Fold Thickness

While all diets showed decreases in skin fold thickness over time (Figure 6), the decrease in average skin fold thickness for cats fed Diet 3 was significantly less than that of the other 2 diets ($P < 0.05$). Thus, cats on Diet 3 had significantly higher skin fold thickness than cats in the other 2 groups. The Cox's proportional hazard model with skin thickness as a time-varying covariate showed a significant relationship between survival and skin thickness (Table 3). Skin thickness was positively correlated with survival, and the hazard ratio was less than 1, indicating that thicker skin was associated with a decreased hazard of dying ($P < 0.05$). The joint longitudinal and survival analysis also showed a significant relationship between both the intercept and slope from the longitudinal model and survival (Table 5), again showing that a higher skin fold thickness is associated with longer survival.

Activity

Longitudinal analysis of activity data, expressed as minutes active per day, showed an overall decrease in activity over time across all diets, but differences between diet groups could not be detected due to

Figure 4. Hemoglobin predicted means (initial age = 7 years).

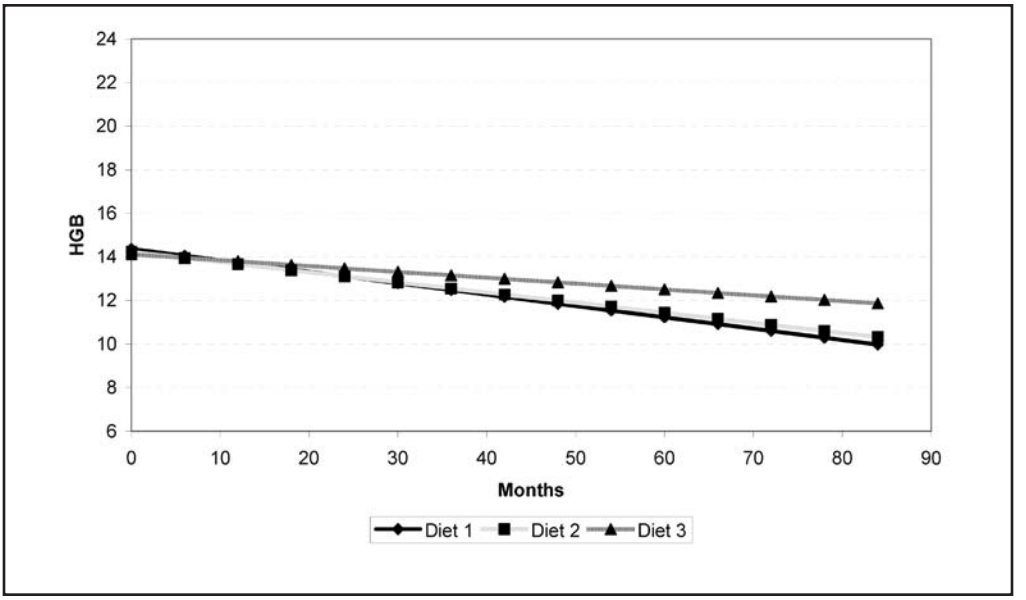
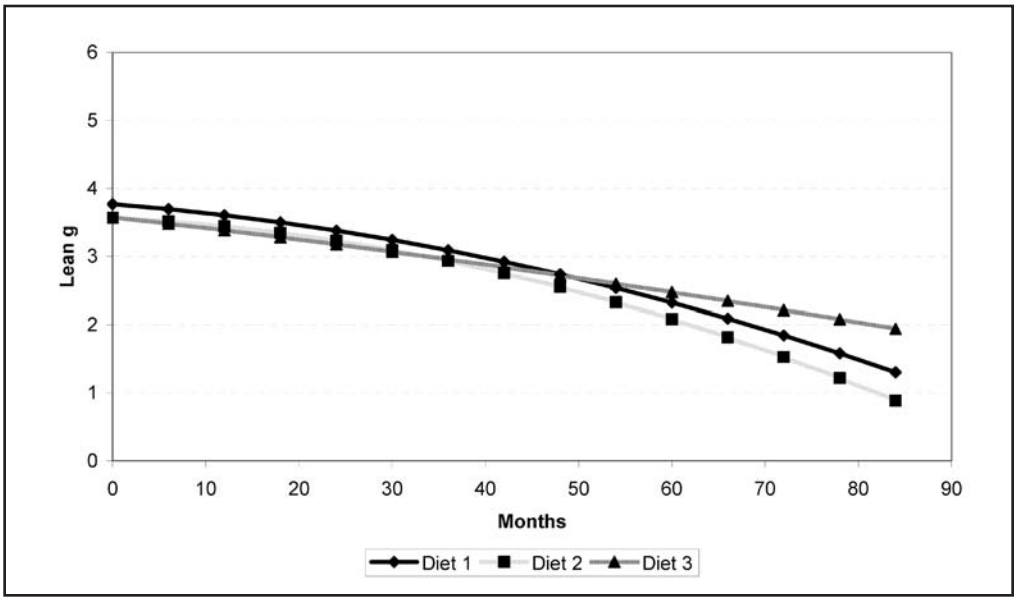


Table 4. Longitudinal analysis results.

		Estimates of Coefficients				
	Diet	Linear	Quadratic	SE	*P* Value	
Red blood cell count	1	-0.04279*		0.00743	Diet 1 vs Diet 2	0.2677
	2	-0.03089*		0.00747	Diet 1 vs Diet 3	0.0184
	3	-0.01807*		0.00659	Diet 2 vs Diet 3	0.2079
Hematocrit	1	-0.08434*		0.03177	Diet 1 vs Diet 2	0.3434
	2	-0.04078		0.03204	Diet 1 vs Diet 3	0.0143
	3	0.02725		0.02837	Diet 2 vs Diet 3	0.1234
Hemoglobin	1	-0.05227*		0.00960	Diet 1 vs Diet 2	0.6743
	2	-0.04650*		0.00965	Diet 1 vs Diet 3	0.0557
	3	-0.02683*		0.00852	Diet 2 vs Diet 3	0.1358
Glucose	1	0.2075*		0.09650	Diet 1 vs Diet 2	0.1485
	2	0.0014		0.09950	Diet 1 vs Diet 3	0.0703
	3	-0.0386		0.08800	Diet 2 vs Diet 3	0.7656
Body weight	1	-0.01593*		0.00769	Diet 1 vs Diet 2	0.6292
	2	-0.01067		0.00764	Diet 1 vs Diet 3	0.8590
	3	-0.01410*		0.00675	Diet 2 vs Diet 3	0.7377
	1		-0.00044*	0.00007	Diet 1 vs Diet 2	0.5856
	2		-0.00050*	0.00007	Diet 1 vs Diet 3	0.0045
	3		-0.00018*	0.00006	Diet 2 vs Diet 3	0.0006
Lean body mass	1	-0.01863*		0.00316	Diet 1 vs Diet 2	0.9077
	2	-0.01914*		0.00306	Diet 1 vs Diet 3	0.5959
	3	-0.01643*		0.00263	Diet 2 vs Diet 3	0.5056
	1		-0.00022*	0.00005	Diet 1 vs Diet 2	0.2954
	2		-0.00030*	0.00005	Diet 1 vs Diet 3	0.0170
	3		-0.00005	0.00005	Diet 2 vs Diet 3	0.0005
Skin thickness	1	-0.01150*		0.00294	Diet 1 vs Diet 2	0.8568
	2	-0.01226*		0.00302	Diet 1 vs Diet 3	0.1134
	3	-0.00507		0.00267	Diet 2 vs Diet 3	0.2629
	1		-0.00032*	0.00007	Diet 1 vs Diet 2	0.8032
	2		-0.00035*	0.00009	Diet 1 vs Diet 3	0.0035
	3		0.00000	0.00008	Diet 2 vs Diet 3	0.0038
Minutes active/day	1	-0.06699*		0.02279	Diet 1 vs Diet 2	0.3861
	2	-0.03733		0.02478	Diet 1 vs Diet 3	0.5609
	3	-0.08565*		0.02208	Diet 2 vs Diet 3	0.1564

*Coefficient significantly different from 0, $P < 0.05$.

Figure 5. Lean body mass predicted means (initial age = 7 years).



the smaller number of animals and large standard errors (Table 4). The Cox's proportional hazard model with activity as a time-varying covariate showed a significant relationship between survival and activity (Table 3). The hazard ratio was less than 1, indicating that greater activity was associated with a decreased hazard of dying ($P < 0.05$). Significant differences between diet groups 1 and 3 were not detected using the joint longitudinal and survival analysis, but there was a trend ($P < 0.10$) to indicate greater activity for cats on Diet 3.

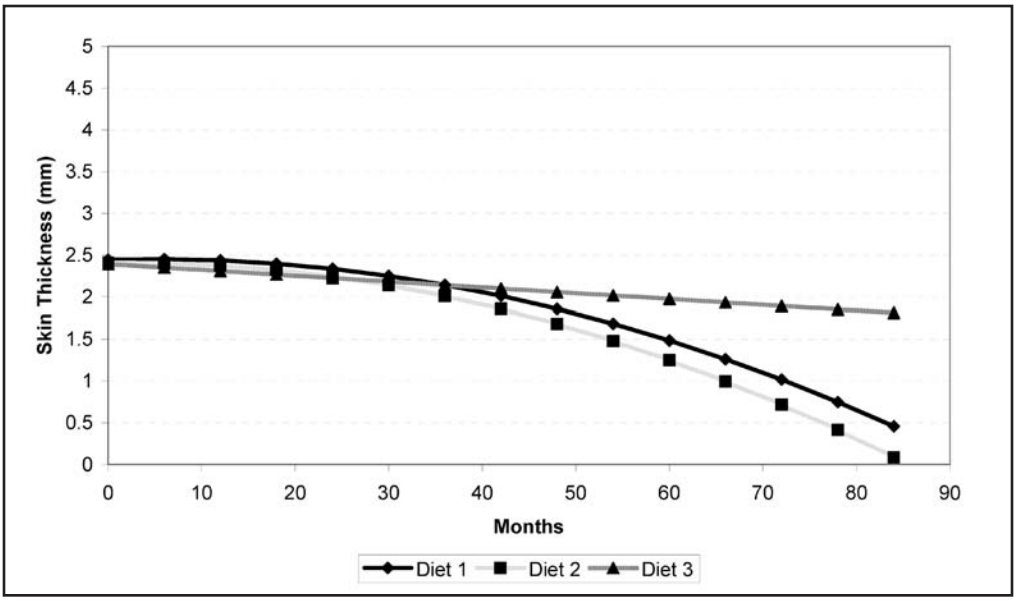
DISCUSSION

The data presented here are highly supportive of the hypothesis that a combination of nutritional interventions could have a positive effect on the health and longevity of senior cats. Cats consuming a diet containing the nutritional blend lived about 1 year longer, on average, than cats fed the control diet. The hazard of dying for the cats on the supplemented diet was only 43% of the hazard of dying for the cats on the control diet, resulting in a longer lifespan.

Previous research in other species has suggested health benefits of the various components of the nutrient blend tested in this study.[8-11,18-21] For example, a recent study in rats showed that lifelong supplementation of a prebiotic (oligofructose-enriched inulin from chicory root) increased lifespan by over 30%.[21] Diet 3, the diet associated with the greatest health benefits in the current study, contained whole chicory root as a source of prebiotic in addition to antioxidants and a blend of essential fatty acids. The health and longevity effects were intermediate for cats only supplemented with antioxidants, confirming the benefit of the additional components of the nutritional cocktail.

A consistent finding over this multi-year feline study was the higher serum vitamin E levels of cats fed Diet 3 over those of cats eating either of the other 2 diets, and greater serum vitamin E levels were positively associated with survival ($P < 0.05$). Vitamin E may be a marker of differences in health status.[22] Aging is associated with higher levels of oxidative stress, and vitamin E plays an important role in protecting against oxidative stress, preventing lipid peroxidation and damage to DNA, muscle, and neurons. In human studies, oxidative stress is lower in elderly subjects with a high antioxidant status, and this has been linked with lower risk

Figure 6. Skin thickness predicted means (initial age = 7 years).



of chronic disease.[23] As previously reported for the cats in this study, those fed the nutrient blend showed a decreased disease incidence and improved intestinal health.[12] Low serum vitamin E as well as low intake of total energy and other specific nutrients has been associated with reduced physical function and increased frailty in the elderly.[22,24] High-circulating vitamin E was associated with lower mortality in a prospective study with over 29,000 older male smokers.[25] Dietary antioxidant supplementation or high intake of foods rich in antioxidants such as vitamins E, C, and beta carotene have been correlated with physical performance and strength measurements in people.[18]

In old dogs, combined supplementation of vitamins E and beta carotene enhanced some measures of immune and oxidative status.[19] In cats with renal insufficiency, supplementation with antioxidant vitamins E, C, and beta carotene significantly reduced DNA damage.[20]

Other parameters in this study that showed significant or near significant relationships with survival were RBC count, HCT, HGB, skin fold thickness, LBM, body weight, and activity levels. All of these parameters have important clinical implications for delaying some of the physiological changes in aging that impact longevity. In addition to improved survival and higher levels of serum vitamin E, cats fed Diet 3 showed slower declines in body weight, LBM, hematological parameters, and skin fold thickness over the last years of their lives.

Anemia from a variety of causes and disease states is common in elderly cats. Even in "healthy" aging, RBC count appears to decrease. In a study comparing young, "healthy old," and "frail old" cats, the healthy old cats showed significantly lower RBC count, HGB, and HCT than young cats, and the average HCT for the frail old cats was significantly lower than the healthy old cats.[26] In the current study, cats on Diet 3 better maintained levels of red cell indices over time compared to cats on the control diet, and these parameters were also significantly related to survival.

Body weight and lean tissue decline in cats over the age of 12, particularly in the last 1 to 2 years of life.[27,28] Cats on Diet 3 showed slower declines in both their body weight and LBM over time compared with cats on the control diet, effects that were also correlated with survival.

Table 5. Joint longitudinal and survival modeling results.

		Comparing Diets 1 and 3		
	Joint Parameters	**Estimate**	**Standard Error**	***P* Value***
Red blood cells	Intercept	0.2065	0.0729	0.0065
	Slopes	9.1837	4.1557	0.0314
Hematocrit	Intercept	0.0427	0.0147	0.0053
	Slopes	1.2842	1.1302	0.2609
Hemoglobin	Intercept	0.1319	0.0520	0.0141
	Slopes	6.4989	3.5949	0.0762
Glucose	Intercept	-0.0323	0.0430	0.4560
	Slopes	0.9473	6.4270	0.8834
Body weight	Intercept	0.1880	0.0699	0.0095
	Slopes	20.4829	4.7507	0.0001
Lean body mass	Intercept	0.1065	0.0827	0.2032
	Slopes	37.9549	6.7829	0.0000
Skin thickness	Intercept	6.1653	2.4128	0.0135
	Slopes	1.0485	0.0042	0.0000
Minutes active/day	Intercept	0.1280	0.0823	0.1290
	Slopes	3.0904	1.6857	0.0755

*For estimate being equal to 0.

The condition of the skin and hair coat often deteriorates in elderly cats, possibly reflecting a deterioration of nutritional status or other physiological changes. In a study comparing young, healthy old, and frail old cats, the frail old cats showed significantly thinner skin compared to young and healthy old cats.[29] Changes in appearance or consistency of the skin and hair coat in older animals can include a rough or greasy hair coat, the presence of flakes or scales, slow wound healing, or increased susceptibility to infections. This could be related to the lipid content of the diet or nutrient absorption.[30-32] Fat digestibility in particular has been shown to be reduced in old cats.[27,33] An adequate level of vitamin E in the diet is important for protecting the skin from oxidative damage as well as providing photoprotection.[34] Higher serum levels of vitamin E seen in this group of cats, or, alternatively, essential fatty acids from the added oils in the diet could have contributed to improved skin health.

The better maintenance of skin fold thickness in cats on Diet 3 is interesting in the context of their concurrent better maintenance of LBM. Skeletal muscle, skin, and internal organs all contribute to LBM and contain the most metabolically active cells in the body,[35] which could be a factor in the increased survival seen in the Diet 3 cats. Similarly, though not statistically significant in the subset of animals tested, the trend for better maintenance of activity levels in these cats could be linked to slower decline in LBM. Further studies using larger numbers of animals are needed to confirm this relationship.

Despite evidence linking dietary antioxidants or physiological antioxidant status with measures of improved health status, results from this study showed that antioxidants alone did not deliver measurable benefits on either survival or other health parameters.

Whether the results from this study reflect the combined benefits of the different dietary interventions or some synergistic effects between the nutrients is not known. Recent studies support the additive benefits of combined nutritional strategies.[8,9] In a

double-blind placebo-controlled study of 100 adults, a combination of a multivitamin supplement with an omega-3 fatty acids supplement reduced circulating levels of homocysteine, triglycerides, and C-reactive protein more than either supplement alone.[8] Supplementation of prebiotics and natural antioxidants into bread positively influenced several parameters of the immune and antioxidant system in 38 men when compared to control or prebiotic-supplemented bread only.[9]

CONCLUSIONS

Results from this study show that senior cats fed a diet containing supplemental antioxidants vitamin E and beta carotene, dried chicory root, and a blend of omega-3 and omega-6 fatty acids lived significantly longer than cats fed a standard nutritionally complete feline diet. Physiological health measures known to decrease with normal aging in cats, such as body weight, LBM, skin thickness, and red cell indices, declined more slowly in cats fed the test diet, and many of these measured parameters were also found to be correlated with survival. As previously reported, cats fed this diet tended to show a decreased disease incidence and improved intestinal health.[12] This suggests that the nutrient blend may provide some protection against certain aging conditions and disease states, contributing to the increased longevity; however, additional research is needed to elucidate the mechanisms for both the increased survival and improvement in health status of these aging cats.

REFERENCES

1. Allen TA: Management of advanced chronic renal failure. In: Kirk RW, ed. *Current Veterinary Therapy X.* Philadelphia, PA: W.B. Saunders; 1989:1195-1198.
2. Chew DJ, Schenck PA, Buffington CAT: Feeding the aging cat with chronic renal failure. *Compend Contin Educ Pract Vet Suppl* 2004;26(Suppl 2A):24-28.
3. Freeman LM: Eat to your heart's content: nutritional modulation of cardiac disease. *Compend Contin Educ Pract Vet Suppl* 2002;24(Suppl 9A):46-49.
4. Michel KE, Hess RS: Advances in the nutritional management of feline diabetes. *Compend Contin Educ Pract Vet Suppl* 2002;24(Suppl 9A):50-55.
5. Cave NJ, Marks SL: Mechanisms and clinical applications of nutrition in inflammatory bowel disease. *Compend Contin Educ Pract Vet Suppl* 2004;26(Suppl 2A):51-57.
6. Harman D: Role of free radicals in aging and disease. *Ann NY Acad Sci* 1992;673:126-141.
7. Jacob RA, Burri BJ: Oxidative damage and defense. *Am J Clin Nutr* 1996;63(Suppl):985S-990S.
8. Earnest CP, Kupper JS, Thompson A, Guo WM, Church TS: Synergistic effects of multivitamin and omega-3 fatty acid supplementation. *FASEB Journal* 2007;21(5):A698.
9. Seidel C, Boehm V, Vogelsang H, et al: Influence of prebiotics and antioxidants in bread on the immune system, antioxidatve status and antioxidative capacity in male smokers and non-smokers. *Br J Nutr* 2007;97:349-356.
10. Das UN: Essential fatty acids as possible enhancers of the beneficial actions of probiotics. *Nutrition* 2002;18:786-789.
11. Gogos CA, Ginopoulos P, Salsa B, Apostolidou E, Zoumbos NC, Kalfarentzos F: Dietary omega-3 polyunsaturated fatty acids plus vitamin E restore immunodeficiency and prolong survival for severely ill patients with generalized malignancy. *Cancer* 1998;82(2):395-402.
12. Cupp CJ, Jean-Philippe C, Kerr WW, Patil AR, Perez-Camargo G: Effect of nutritional interventions on longevity of senior cats. *Intern J Appl Res Vet Med* 2006;4(1):34-50.
13. Breen R: Regression model: censored, sample-selected, or truncated data. Sage University Paper series on Quantitative Applications in the Social Sciences. Thousand Oaks, CA: SAGE 07-111; 1996.
14. Allison PD: *Survival Analysis Using the SAS System: A Practical Guide*. Cary, NC: The SAS Institute Inc.; 1995.
15. Verbeke G, Molenberghs G: *Linear Mixed Models for Longitudinal Data*. New York, NY: Springer-Verlag; 2000.
16. Guo X, Carlin BP: Separate and joint modeling of longitudinal and event time data using standard computer packages. *Am Stat* 2004;58(1):16-24.
17. SAS: *SAS/STAT User's Guide. Version 9.1*. Cary, NC: The SAS Institute Inc.; 2003.
18. Cesari M, Pahor M, Bartali B, et al: Antioxidants and physical performance in elderly persons: the Invecchiare in Chianti (InCHIANTI) study. *Am J Clin Nutr* 2004;79:289-294.
19. Park JS, Hayek MG, Reinhart GA, Massimino S, Chew BP: Beta-carotene and vitamin E supplementation on immunity and oxidative status in geriatric dogs. *FASEB Journal* 2007;21(5):A49.
20. Yu S, Paetau-Robinson I: Dietary supplements of vitamins E and C and b-carotene reduce oxidative stress in cats with renal insufficiency. *Vet Res Comm* 2006;30:403-413.
21. Rozan P, Nejdi A, Hidalgo S, Bisson JF, Desor D, Messaoudi M: Effects of lifelong intervention with an oligofructose-enriched inulin in rats on general health and lifespan. *Br J Nutr* 2008:1-8. Published online April 11, 2008.

22. Bartali B, Frongillo EA, Guralnik JM, Stipanuk MH, Allore HG, Cherubini A, Bandinelli S, Ferrucci L, Gill TM: Serum micronutrient concentrations and decline in physical function among older persons. *JAMA* 2008;299:308-315.
23. Buijsse B, Feskens EJM, Schlettwein-Gsell D, et al: Plasma carotene and α-tocopherol in relation to 10-y all-cause and cause-specific mortality in European elderly; the Survey in Europe on Nutrition and the Elderly, a Concerted Action (SENECA). *Am J Clin Nutr* 2005;82:879-886.
24. Ble A, Cherubini A, Volpato S, et al: Lower plasma vitamin E levels are associated with the frailty syndrome: The InCHIANTI study. *J Gerontol* 2006;61A:278-283.
25. Wright ME, Lawson KA, Weinstein SJ, et al: Higher baseline serum concentrations of vitamin E are associated with lower total and cause-specific mortality in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. *Am J Clin Nutr* 2006;84:1200-1207.
26. Czarnecki-Maulden G, Cupp CJ, Patil AR, Perez-Camargo G: Effect of aging on blood metabolites in the cat. *Compend Contin Educ Pract Vet Suppl* 2004;26(Suppl 2A):74.
27. Perez-Camargo G: Cat nutrition: what is new in the old? *Compend Contin Educ Pract Vet Suppl* 2004;26(Suppl 2A):5-10.
28. Perez-Camargo G, Patil AR, Cupp CJ: Body composition changes in aging cats. *Compend Contin Educ Pract Vet Suppl* 2004;26(Suppl 2A):71.
29. Czarnecki-Maulden G: Unpublished data, 2008.
30. Rivers JPW, Frankel TL: Fat in the diet of cats and dogs. In: Anderson ES, ed. *Nutrition of the Dog and Cat.* Oxford: Pergamon Press; 1980:67-99.
31. Rivers JPW: Essential fatty acids in cats. *J Small Anim Pract* 1982;23(9):563-576.
32. MacDonald ML, Anderson BC, Rogers QR, Buffington CA, Morris JG: Essential fatty acid requirements of cats: pathology of essential fatty acid deficiency. *Am J Vet Res* 1984;45:1310-1317.
33. Patil A, Cupp C, Perez-Camargo G: Incidence of impaired nutrient digestibility in aging cats. *Compend Contin Educ Pract Vet Suppl* 2004;26(Suppl 2A):72.
34. Shapiro SS, Saliou C: Role of vitamins in skin care. *Nutrition* 2001;17:839-844.
35. Laflamme DP: Nutrition for aging cats and dogs and the importance of body condition. *Vet Clin Small Anim* 2005;35:713-742.