



## Incidence of canine dilated cardiomyopathy, breed and age distributions, and grain-free diet sales in the United States from 2000-2019: A retrospective study.

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DISCLAIMER: The data shown in our presentations, like the majority of data presented at this FDA colloquium, is preliminary. The initial study presented here, is currently undergoing peer review. The other studies (taurine/carnitine, and anti-nutrient factors) share preliminary data that are part of a larger study. We would like to thank Kansas State CVM for allowing us to present this data and would like to emphasize that while this colloquium raises more questions than answers, the connections and collaborations that were forged will help to understand the link between diet and DCM.

Further information on research from BSM Partners can be found on:

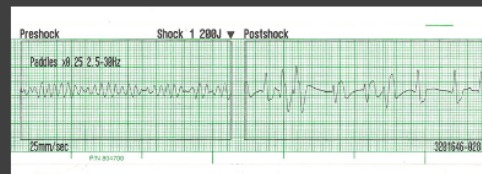
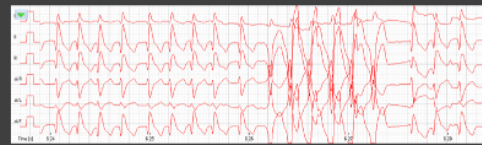
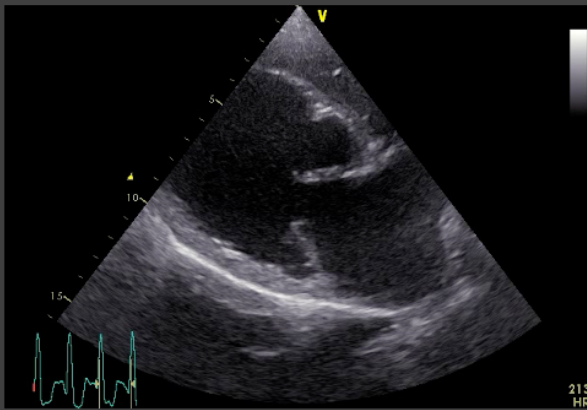
**[www.dcmresearchproject.org](http://www.dcmresearchproject.org)**



### Disclosures:

This study was independently funded by BSM Partners, a full-service pet food consulting firm.

## BACKGROUND: DCM is a disease of the myocardium



Oxford EM, et al, *J Am Vet Med Assoc.* 2018;252(4):415-418.  
doi:10.2460/javma.252.4.415



Dilated cardiomyopathy is a disease of the myocardium, which, as shown in this echocardiographic movie, results in thinning of the heart, decreased pump function, and leading to congestive heart failure, dangerous arrhythmias, and sudden cardiac death.

**BACKGROUND:** Historically, DCM was considered an inherited disease; other etiologies are also recognized.



Dilated Cardiomyopathy is the most common cardiomyopathy in the dog, and has historically been considered to be an inherited disease of high prevalence in certain breeds, including the GD, Doberman, and Irish Wolfhound. Other breeds have also been identified as having an inherited component, as noted in this slide.

In addition to hereditary causes, any breed can develop a DCM phenotype with concurrent hypothyroid disease, nutritional deficiencies, chronic tachycardia, or myocarditis can also lead to a DCM phenotype. Because a definitive etiology is often unknown in the absence of histopathology, the best way to describe the condition is “DCM phenotype”

BACKGROUND: Is the incidence of DCM increasing in the US?

- Has the annual incidence of DCM increased over the past 10+ years?
- Are there a higher number of breeds without a known inherited predisposition diagnosed with DCM phenotype now than were accounted for in the past?
- How many dogs eat grain-free dog food, and has this number increased over the past decade?



## HYPOTHESIS

We hypothesized that we could determine the incidence, breed, and age distributions of dogs diagnosed with DCM among veterinary cardiologists in the US through a retrospective survey. This would allow us to determine if a correlation to increased grain-free dog food sales existed.



## Study Design: Retrospective survey

Annual DCM Incidence = New Canine DCM Phenotype / Total Initial Canine Cases

- Cases were evaluated by a board certified/residency trained veterinary cardiologist or resident.
- Cases were diagnosed by echocardiography using standard reference ranges, as reported by the diagnosing cardiologists.
- DCM incidence data and breed distribution were analyzed using linear regression analyses.
- Annual age distribution was plotted and evaluated in reference to:
  - Age at DCM diagnosis
  - Age at other cardiac diagnosis
  - Age of all canines presenting to hospital





## Study Design: Retrospective survey

### Breed Distribution

- Breeds with DCM phenotype were documented each year.
- 68 breeds were identified from 3 practices.
- Breeds were placed in the following categories and organized by year:

#### Inherited

Doberman  
Great Dane  
Boxer  
St. Schnauzer  
Irish Wolfhound  
Dalmatian  
PWD  
Cocker Spaniel  
Old Eng Sheepdog  
English Bulldog

#### Retrievers

Labs  
Goldens  
Ches.Bay

#### Small Breed <30lb

Min Poodle  
Min Schnauzer  
Jack Russell  
Pomeranian  
Boston Terrier  
CKCS  
Sheltie  
Coton de Tulear  
Irish Terrier  
Yorkie  
Whippet

#### Other Breeds

German Shepherd  
Mastiff  
American Bulldog  
Border Collie  
Standard Poodle  
St Bernard  
English Setter  
GSHP  
Borzo  
Beauceron  
+ others

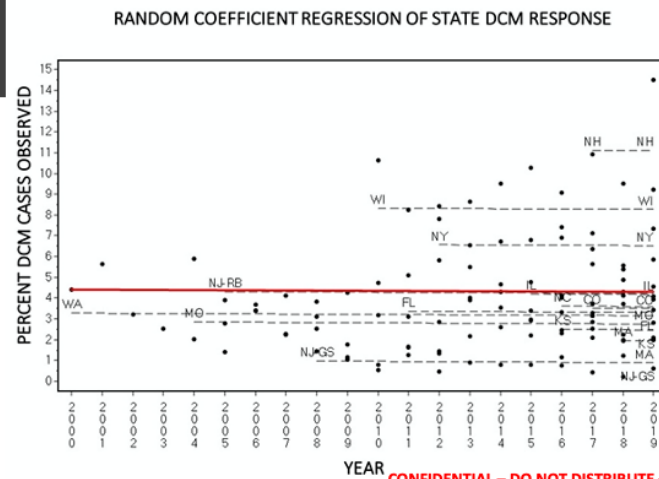
#### Mixed Breed

#### Not Specified

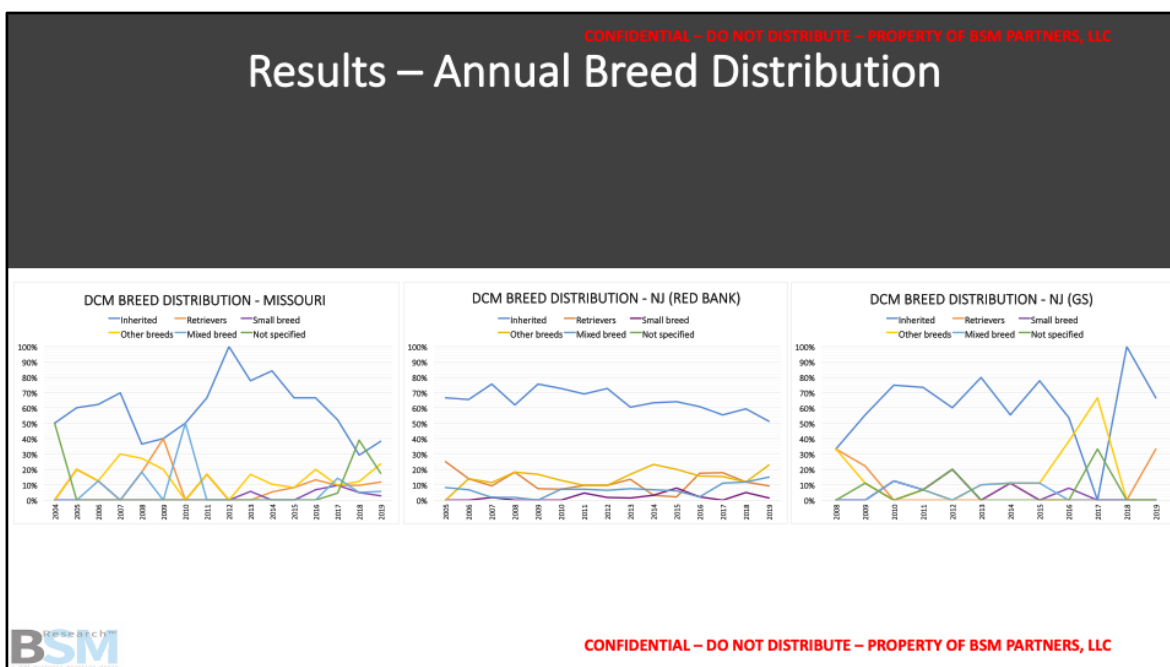


## Results: Linear Regression Analysis – DCM Incidence

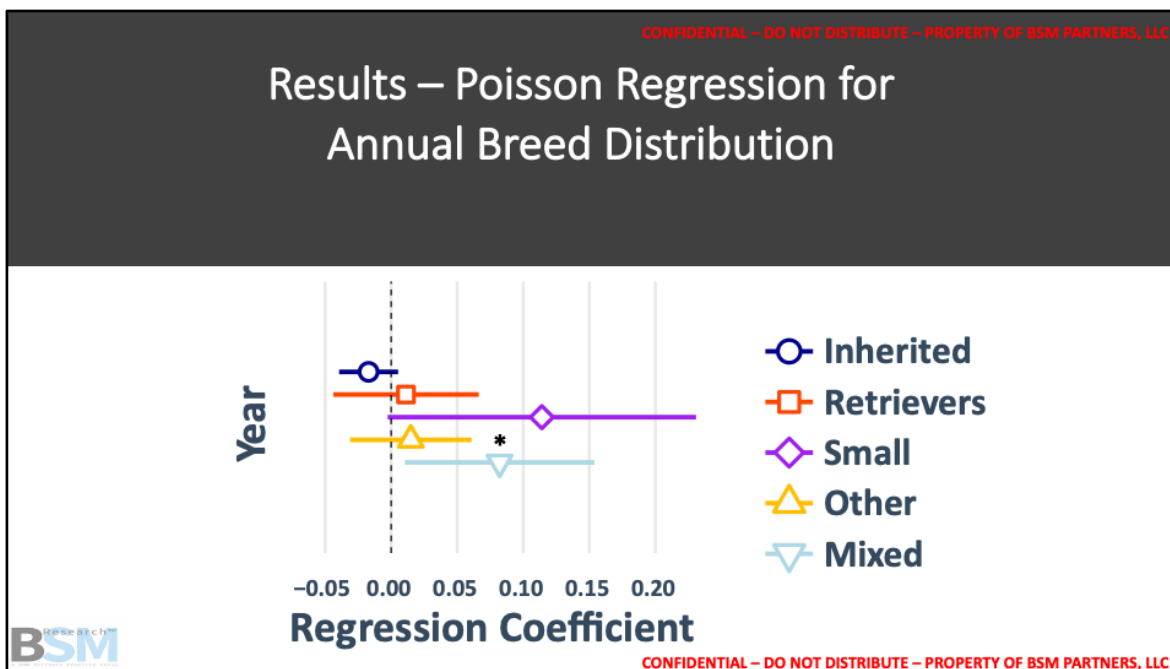
Average Annual DCM  
Incidence (by  
cardiologists):  
3.83%  
2.41-5.85  
STDV +/- 0.77%



This graph displays the results of a mixed model random coefficient regression analysis including all services with the exception of Ethos- Hawaii (only one data point). For all states over all years, the average annual DCM Incidence rate was 3.83%. Black points indicate percent DCM per service each year. Trend - lines for each service are shown as black dashed lines. **The best fitted regression model is shown in red.** This trend line does not support a change in DCM incidence over time among cardiology services that participated in this study.

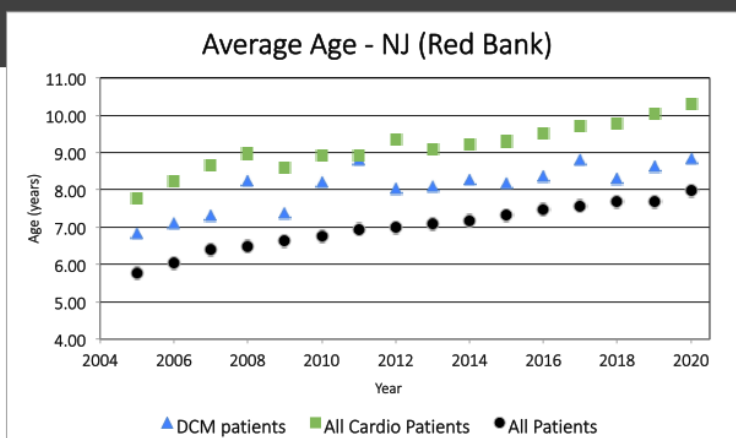


Here, scatter plots represent annual breed distributions from 3 different cardiology services: University of Missouri, Red Bank, and Garden State. Breeds with a known genetic link to DCM (Inherited group – dark blue) are the most commonly diagnosed with DCM, with all other categories generally being represented less frequently each year, in all three hospitals.



The number of dogs in each group was regressed against year, total DCM cases, and site. Open icon denotes regression coefficient, with matching horizontal lines representing individual confidence intervals. Mixed breeds (light blue) showed a slightly increased trend over the past 15 years, which was statistically significant ( $p=0.025$ , RC 0.082). Small breeds (purple) and other breeds (yellow) showed a statistical trend that was not significant (small breeds:  $p=0.055$ , RC 0.114; other breeds:  $p=0.053$ , RC 0.015). Retrievers (red) did not show a trend over the years ( $p=0.689$ , RC 0.0112). Inherited breeds (dark blue) showed a slight negative trend, which was not significant ( $p=0.134$ , RC -). These results support what some cardiologists have noted – that there seems to be an increase in mixed breed and small breed dogs developing DCM phenotype. However, these data do not evaluate changes in popular breeds over time, infectious disease distribution, or other possible underlying causes.

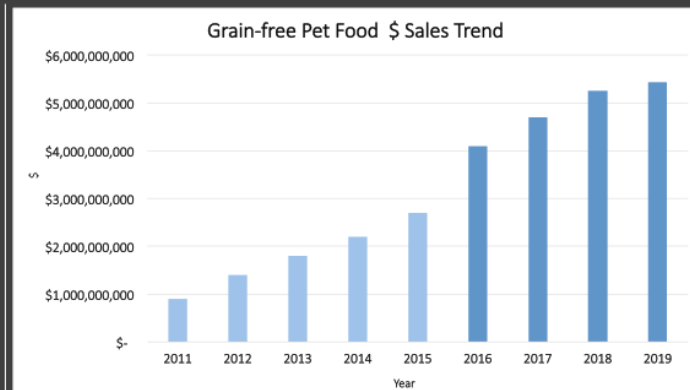
## Results: Annual Average Age Distribution – DCM, All Cardio, All Patients



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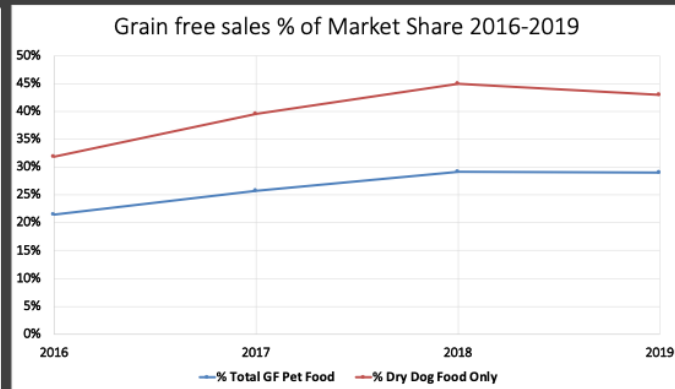
This graph shows age distribution of patients from Red Bank Veterinary Hospital (Tinton Falls) from 2005-2020. Blue triangle depicts the average age of patients at time of DCM diagnosis, green squares depict patients at time of other cardiovascular diagnosis, and black circles denote age of patients at the time of presentation for non-cardiac services. Within all three groups, there is an upward trend in age over the past 15 years. In general, patients diagnosed with DCM are one year older than the general population of canines presenting to the hospital, and one year younger than patients with an alternative cardiac diagnosis. Simply put, these data suggest that dogs with DCM phenotype, as well as the general population are staying healthier for longer.

**Results:**  
**Grain- Free Pet**  
**Food \$ Sales**  
**2011-2019**



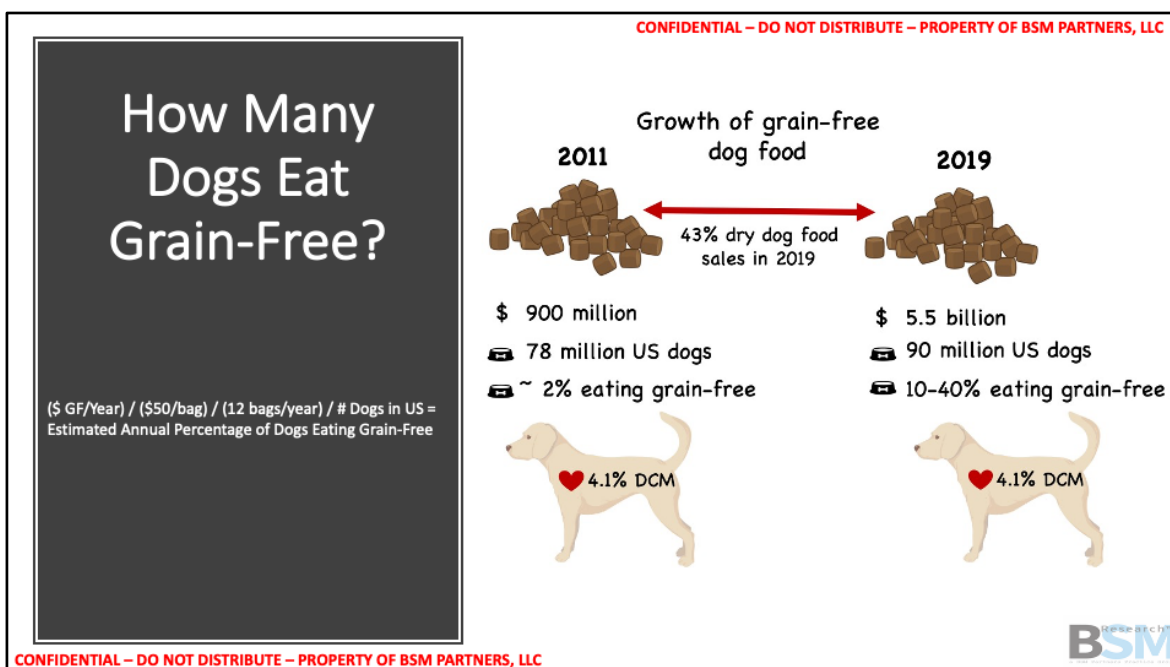
Finally, Grain-free pet food sales data provided by the Nielsen company, xAOC, and Petco & Petsmart, and used with permission. This bar chart denotes grain-free pet food sales from 2011-2019. Grain-free pet food sales reached \$900,000,000 in 2011, the first year that grain-free pet food sales were recorded. By 2019, sales had grown to \$5,426,879,686. Light blue bars denote grain-free pet food sales through pet specialty retail stores only (2011-2015). Dark blue bars denote sales through brick and mortar food, drug, mass, and convenience stores *in addition to* pet specialty stores. These numbers are an underestimate of grain-free pet food sales, as sales through farm and feed stores, veterinary clinics, other stores selling pet foods, and online sales are not included.

**Results:**  
**Grain- Free Pet Food**  
**% Market Share**  
**2016-2019**



xAOC, Petco  
& PetsMart

This graph shows percent market share of grain-free pet food sales from 2016-2019. The blue line includes total grain-free pet food as a percent of the total pet food market. The red line denotes the percent of kibble that is grain-free from 2016-2019, and this number reached 43% in 2019.



Here is a model, which estimates the percentage of dogs eating grain-free diets in 2011, compared to 2019. The percentage of dogs eating grain-free diets in 2011 was calculating using the following formula: **\$900,000,000 grain-free sales / \$50.00 per bag / 12 months / 78,000,000 dogs = 2%**. The percentage of dogs eating grain-free diets in 2019 was calculated using the same formula, adjusted for the number of dogs and dollar sales in 2019: **\$5,500,000,000 grain-free sales / \$50.00 per bag / 12 months / 90,000,000 dogs = 10%**. These numbers are likely underestimates, as dollar sales do not include all sales of grain-free diets.

**The bottom line is that there is no way to calculate the exact number of dogs eating grain free diets. However, these available data suggest that there has been at least a 5-fold increase – from 2-10% in dogs eating grain free diets. Furthermore, if we consider the % market share data from the past 4 years, it is possible that as many as 40% of dogs are eating grain free diets today.**

This huge increase in popularity in these diets over the past decade does not correlate to the relatively stable overall incidence of canine DCM.



## Conclusions

1. The data do not support an increase in the overall incidence of DCM across the US over the past 10+ years.
2. Additionally, the data do not support a correlation between overall incidence of DCM and the increase of grain free pet food sales from 2011-2019.
3. A significant upward trend was noted in mixed breed dogs diagnosed with DCM over the past 15 years.
4. The average age of dogs at the time of DCM diagnosis is increasing – following trends in the general dog population (living healthier for longer)



## Conclusions

An increase in grain-free pet food sales over the past decade represents an increased probability that dogs with DCM phenotype will be eating grain-free foods.

Our data do not support a correlation between grain-free dog food and DCM phenotype.

Further studies are indicated to determine whether smaller cohorts have specific dietary needs independent of diet.



# Thank You

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BSM Partners DCM Research Team





## Evaluation of plasma, whole blood and cardiac muscle taurine and carnitine concentration in purpose-bred mongrel dogs.

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1. BSM Partners, Bentonville, AR
2. University of Missouri, College of Veterinary Medicine, Colombia, MO



**Disclosures:** This research was supported by several companies across various industries, all of whom have an interest in improving canine health.

## BACKGROUND

- Plasma carnitine does not correlate with myocardial concentrations<sup>1,2,3</sup>
- Little is known about how plasma and whole blood taurine concentrations correlate with myocardial concentrations<sup>4</sup>

## OBJECTIVE

To determine whether myocardial taurine and carnitine levels will correlate with:

- Fasted plasma and whole blood taurine
- Fasted plasma carnitine

## Study Design

- 36 dogs (18 M, 18F)
- Fed a commercially available chicken and grain - based diet
- Fasted for 18-24 hours
- Whole blood taurine and plasma taurine and carnitine samples obtained and submitted
- Dogs anesthetized in accordance with approved Animal Care and Use Protocols & endomyocardial biopsies obtained from right ventricle



Plasma and whole blood taurine to UC Davis and Tissue and plasma carnitine samples sent to UC San Diego



## Results - Taurine:

### WB Taurine:

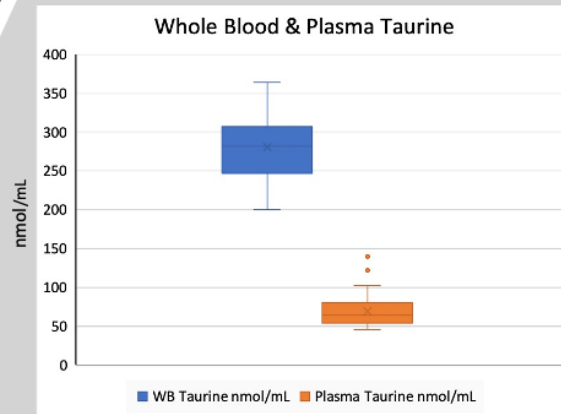
Median: 282 nmol/mL

Range: 200-356

### Plasma Taurine:

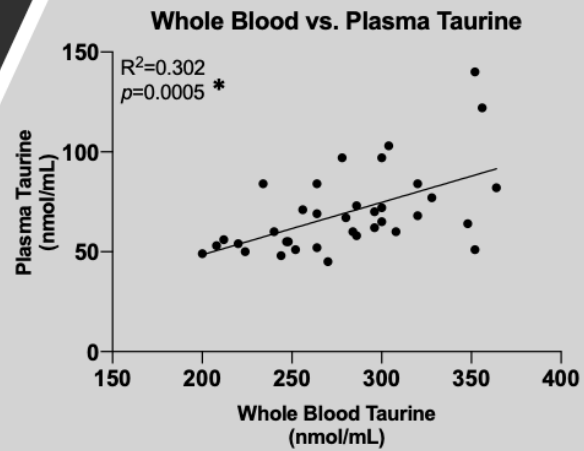
Median: 64.5 nmol/mL

Range: 45 -140



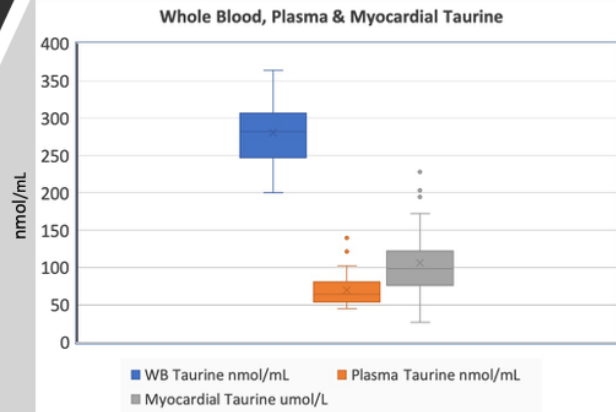
## Results - Taurine:

Fasted whole blood and plasma taurine concentrations are significantly correlated



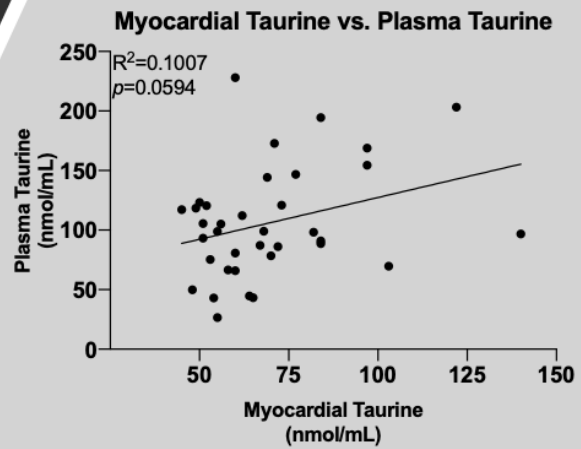
## Results - Taurine:

Myocardial Taurine:  
Median: 98.6 nmol/mL  
Range: 26.6–228.1 nmol/mL

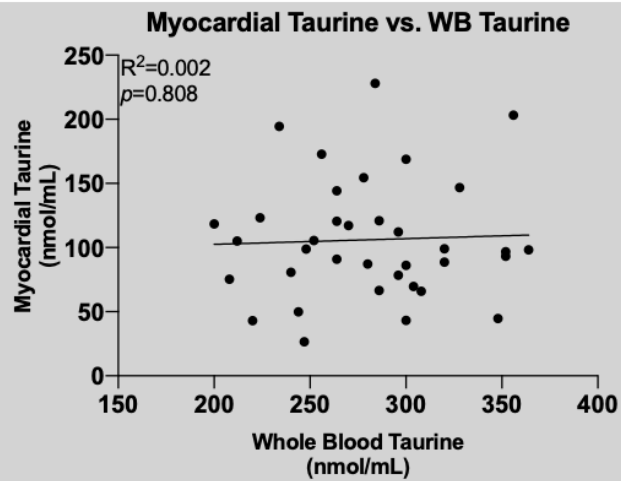


## Results - Taurine:

Weak correlation  
between *fasted*  
plasma taurine  
and myocardial  
taurine  
concentrations



## Non-Significant Taurine Correlations



Plasma and whole blood taurine to UC Davis and Tissue and plasma carnitine samples sent to UC San Diego

## Results - Carnitine:

Plasma free carnitine:

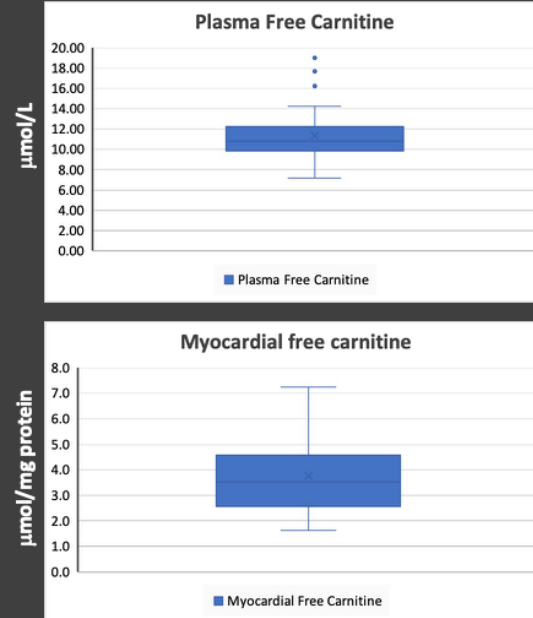
Median: 10.82  $\mu\text{mol/L}$

Range: 7.2-19

Myocardial free carnitine:

Median: 1.4  $\mu\text{mol/mg protein}$

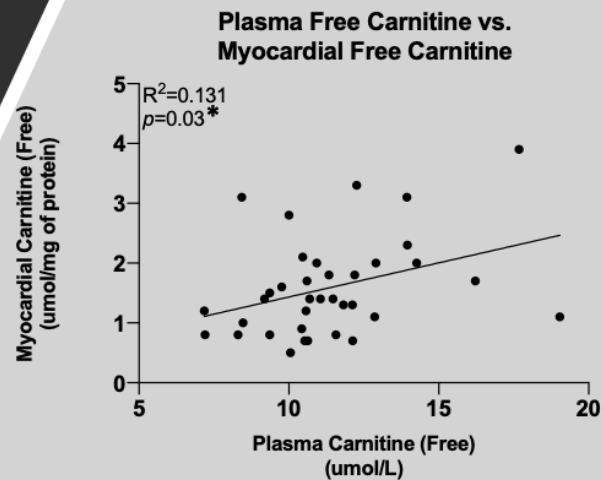
Range: 0.5 -3.9



## Results - Carnitine:

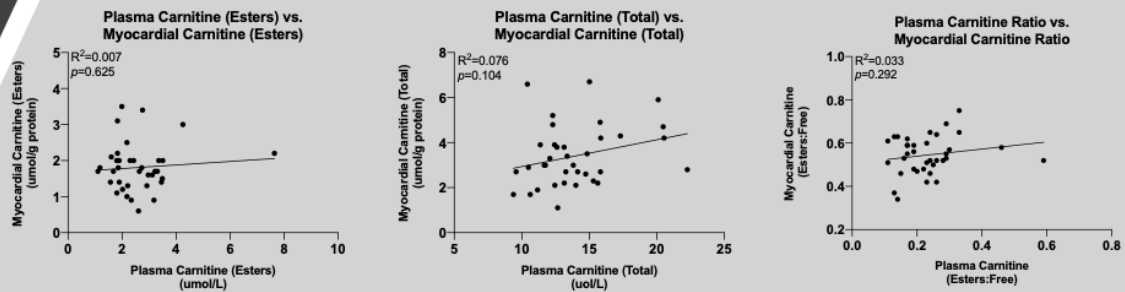
Fasted plasma and myocardial free carnitine are significantly correlated

Clinically significant?



None of the correlations between plasma carnitine and myocardial carnitine are very strong however, the strongest relationship is between free plasma carnitine and myocardial carnitine with a R squared value of 0.131 and a p-value of 0.03.

## Non-Significant Carnitine Correlations



Plasma and whole blood taurine to UC Davis and Tissue and plasma carnitine samples sent to UC San Diego



## Conclusions

- Fasted samples of plasma free carnitine correlate most closely with myocardial free carnitine concentrations
- Fasted plasma taurine concentrations correlate most closely with myocardial taurine concentrations.
  - These correlations are weak however, may be improved with further sampling which will be obtained as the study progresses.
- Important to note these results are obtained from fasted samples.  
**Without fasted samples it is unclear how these values would correlate.**
- Interestingly, there were no significant correlations between any other parameters evaluated including **myocardial and whole blood taurine**



## Acknowledgements:

- Dr. Charles Danko: Statistics
- Dr. Sydney McCauley & BSM Partners Team



## References

- 1) Keene, B. W., D. P. Panciera, C. E. Atkins, V. Regitz, M. J. Schmidt, and A. L. Shug. 1991. Myocardial l-carnitine deficiency in a family of dogs with dilated cardiomyopathy. *J. Am. Vet. Med. Assoc.* **198**(4):647–650.
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- 4) Sanderson, S.L., Gross, K.L., Ogburn, P.N., Calvert, C., Jacobs, G., Lowry, S.R., Bird, K.A., Koehler, L.A., Swanson, L.L. 2001. Effects of dietary fat and L-carnitine on plasma and whole blood concentrations and cardiac function in healthy dogs fed protein-restricted diets. *Am Journ Vet Res.* **62**(10): 1616-1623.

## Role of formulation and processing on nutrients and anti-nutrient factors during small scale commercial extruded kibble manufacturing

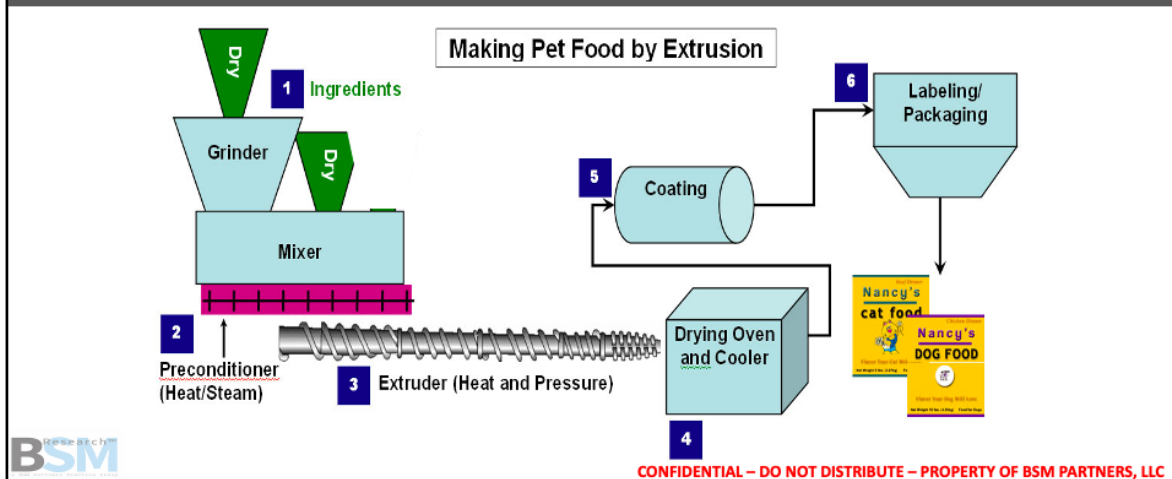
- Stephanie D. Clark, PhD, CVT, PAS<sup>1</sup>
- Renee Streeter, DVM, DACVN<sup>1</sup>
- David Perez, BS<sup>1</sup>
- Sydney R. McCauley, PhD, PAS<sup>1</sup>
- Bradley Quest, DVM<sup>1</sup>
- and
- Shiva Garimella, PhD, CFS, PAS\*<sup>1</sup>

**1. BSM Partners, Bentonville, AR**



**Disclosures:** This research was supported by several companies across various industries, all of whom have an interest in improving canine health.

## Do small scale processing plants impact the final product?



Points to be made:

1. Common Unit Operations across all manufacturers
2. Do raw materials impact finished product?
3. Does processing impact finished product?
4. Does having more of animal protein impact processing or does processing impact starch of one source more than other?

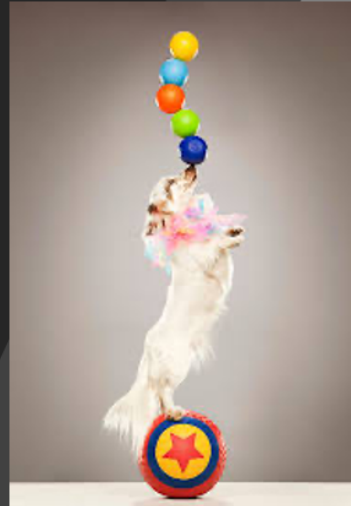
## HYPOTHESIS

We hypothesized that **nutrient profiles** and **Anti-Nutritional Factors (ANF)** of finished **kibble** were **not affected** by ingredient composition or size of manufacturing plant.



## Objectives

- To evaluate the **role of formulation** on extrusion processing parameters
- To evaluate **role of processing** on changes in nutrients and anti-nutritional factors during commercial extrusion process
- To evaluate whether quality of diet is a function of the size of the manufacturer





## Study Design

### 2 x 2 Factorial Design

Protein/Starch Source	Grains	Legumes/Tuber
High Animal Protein	G-Hi (1)	L-Hi (3)
Low Animal Protein	G-Low (2)	L-Low (4)

Diet 1: Grain – Grain Animal Protein

Diet 3: Legume – High Animal Protein

Diet 2: Grain – Low Animal Protein

Diet 4: Legume – Low Animal Protein

Diet 5: Purina Dog Chow – Chicken Adult



Diet 5 is a commercially manufactured widely available whole grain diet.

## Formulation Overview

Proximate	% (Dry Matter)	g/Mcal
Moisture, Max	10.0	
Protein, Min	28.0	70.0
Fat, Min	15.0	37.5
Fiber, Max	3.75	9.4

Diets 1-4 were formulated in collaboration with a Board-Certified Veterinary Nutritionist, to exceed AAFCO's requirements for Adult Maintenance



Each diet were formulated to have same macro nutrient profile.

## Sample Collection Points

1. Blender

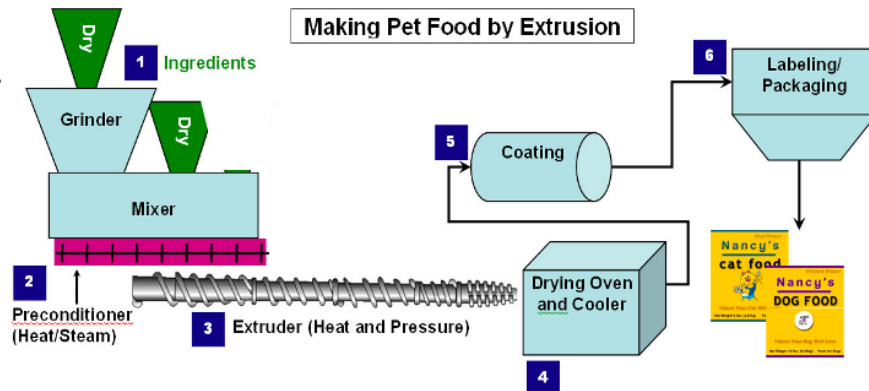
2. Preconditioner

3. Extruder

4. Dryer

5. Coater

6. Storage



Storage: 3, 9, 12 and 18 months.

## Analysis Performed - Nutrients

### *Full AAFCO Analysis*

- ✓ *Proximates*
- ✓ *Fatty Acids*
- ✓ *Amino Acids*
- ✓ *Vitamins*
- ✓ *Minerals*

- ✓ *Starch Profile*
- ✓ *Sugar Profile*
- ✓ *Fiber Profile*
- ✓ *Flour Particle Size Analysis*

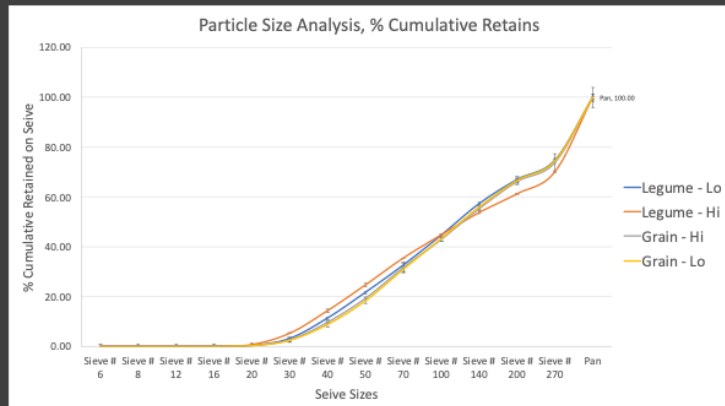


## Analysis Performed – Anti Nutrients

- ✓ *Heavy Metals*
- ✓ *Resistant Starch*
- ✓ *Toxins & Myco-toxins*
- ✓ *Anti-nutritional Factors (Lignin, Phytic Acid, Lectins\*)*
- ✓ *Nitrates And Nitrites*
- ✓ *Oxidative Rancidity Products*



## Particle Size Analysis

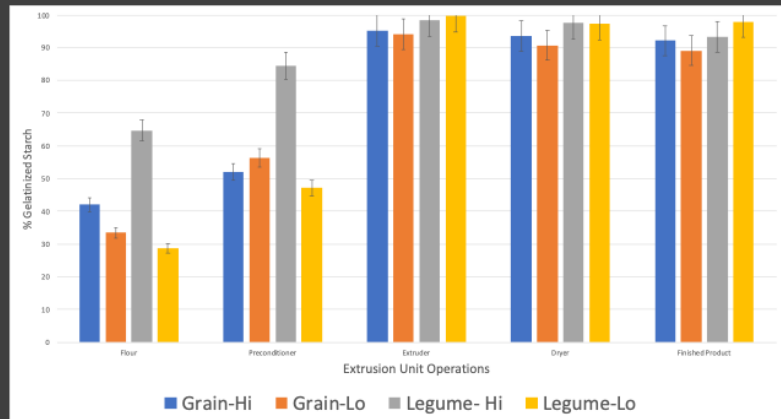


NOTE: Uniform particle size distribution helps for even thermal and mechanical energy distribution during extrusion process



All the flours have been processed using same hammer mill settings.

## Starch Gelatinization



non-grain ingredients

## Impact of Processing on Nutrients

NUTRIENT ANALYZED	RESULTS
Proximates	NO change among diets 1-4 ( $p > 0.05$ )
Sugars	NO detectable levels of simple sugar after extrusion
Amino Acids	Reduction in lysine
Vitamins	The greatest effect of extrusion was seen on Vitamins
Minerals	NO change among diets 1-4 ( $p > 0.05$ )



## Impact of Processing on Anti-Nutrients



### ANF Analyzed

### Results

Lignins and  
Phytic Acid

- ✓ Lignins were not detectable (i.e. <0.5%)
- ✓ Phytic acid was <1.0%.

Short Chain  
Carbohydrates

- ✓ Legume/Tuber based formulations contained low levels of Stachyose and Raffinose
- ✓ Extrusion processing did not significantly impact these carbohydrates.

Resistant  
Starch (RS)

- ✓ Low levels of RS (<5.0%) were found in flour samples
- ✓ Diets 1, 3 and 4 no detectable levels in finished product
- ✓ Diet 2 (Grain Lo) had 1.1% in finished product

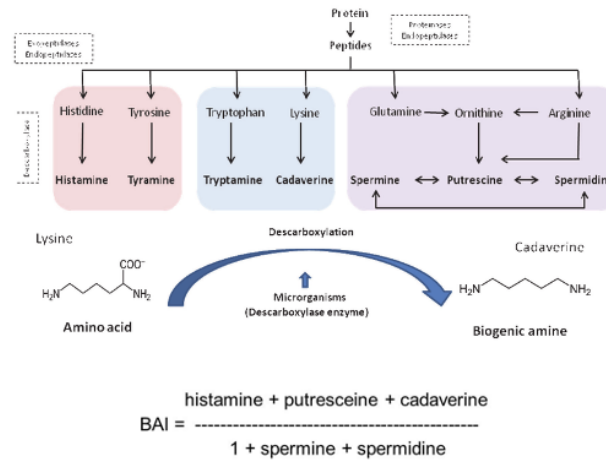
Flour didn't have any Lignin, and no lignin was found after processing.

## Impact of Processing on Anti-Nutrients

Anti-Nutrients Analyzed	Results
Toxins	✓ No Aflatoxin (B1, B2, and G2), Ochratoxin, or Zearalenone
Heavy Metals	✓ No Arsenic, Lead or Mercury
Biogenic Amines (BA)	✓ Biogenic amine index in all four finished products was < 2.0. ✓ Extrusion had no impact on BA



# Biogenic Amines – Overview



Examples for Biogenic Amines – Histamine, Putrescine, Spearmidine,

- Biogenic Amine of our products will be monitored at 3, 9, 12, 18 months.
- Extrusion had no impact Biogenic Amines, which makes it vital to select right ingredients.
- Biogenic amines are resistant to heat treatment applied in food processing. Therefore, BAs have been considered as good indicators of freshness and spoilage, inferring the quality of fresh and processed food products, thus reflecting the raw-material quality and hygienic conditions during processing

## Biogenic Amines

Diet	Biogenic Amine Index
G-Hi (1)	< 2
G-Low (2)	< 2
L-Hi (3)	< 2
L-Low (4)	< 2
Purina Dog Chow – Chicken Adult	8.8



Diet 5 is a commercially manufactured widely available whole grain diet.

## Conclusions

- Protein, fat, vitamin, and mineral content of all diets (1-5) exceeded AAFCO requirements for Adult Maintenance.
- ANF (lignins and phytates) were not detectable in diets 1-4; however, diet 5 had lignin detectable at 2.2% (N <0.5%) on a dry matter basis (finished product).



- For all the Nutrients, Diets 1-4, were similar to Commercial Diets, however, it was the Anti-nutrients that were different.
- Our data shows that when produced under controlled conditions size of manufacturer doesn't
- This small-scale pet food manufacturer has the capacity to procure raw materials at level better or equal to national level brand.
- Biogenic Amine of our products will be monitored at 3, 9, 12, 18 months.

## Conclusions

- Biogenic amine index was <2.0 in diets 1-4 (small scale manufacturer) and 8.8 in diet 5 (large scale manufacturer)
  - (<2, acceptable, >10, advanced decomposition).
- These data support that this small-scale manufacturer has the capacity to procure raw materials at a level equal to or better than a national level brand.



- For all the Nutrients, Diets 1-4, were similar to Commercial Diets, however, it was the Anti-nutrients that were different.
- Our data shows that when produced under controlled conditions size of manufacturer doesn't
- This small –scale pet food manufacturer has the capacity to procure raw materials at level better or equal to national level brand.
- Biogenic Amine of our products will be monitored at 3, 9, 12, 18 months.

Thank You