

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

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Short title: DCM incidence, breed and age distributions, and grain free diet sales in dogs from
2000-2019.

Abstract

Background: Dilated cardiomyopathy (DCM) is considered a predominantly inherited disease in dogs. Recent reports suggest an increased incidence of DCM in atypical breeds eating grain-free and/or legume-rich diets. However, little data regarding incidence of DCM within the US is available; and no existing data quantifies DCM among breeds over time.

Hypothesis: We hypothesized that DCM incidence among breeds could be estimated by retrospective polling of veterinary cardiologists. Further, if a correlation existed between grain-free diets and DCM, an increase in DCM would be on trend with increased grain-free pet food sales.

Materials and Methods: Thirty-six U.S. cardiology specialty practices were asked for all initial canine and DCM cases evaluated from 2000-2019; fourteen cardiology practices participated. DCM signalment data was provided by three hospitals over 15 years; representing 68 breeds. Age distribution of DCM cases upon diagnosis were compared to other cardio cases and general hospital population from one hospital. All data were evaluated using linear regression models. Grain-free pet food sales data was evaluated from 2011-2019.

Results: Fourteen hospitals participated and reported 67,243 unique canine patients. Nationally, data did not support a significant change in percent DCM over time ($p=0.85$). The overall average incidence rate of DCM during the study period was 3.83% (range 2.41-5.65%), while grain-free diet sales increased 500% from 2011- 2019. No correlation between overall DCM incidence and grain free diet sales was discovered. A significant upward trend in mixed breeds diagnosed with

DCM, with no significant trend in other breeds was appreciated. An upward trend in age at DCM diagnosis was identified, correlating with trends from overall hospital populations.

Conclusions: These data do not support overall increased DCM incidence, or a correlation with grain-free pet food sales. Additional data are necessary to understand whether regional factors contribute to increased DCM within smaller cohorts.

Introduction

Dilated cardiomyopathy (DCM) is the second most common acquired cardiac disease and the most common cardiomyopathy in the dog and is an important cause of canine morbidity and mortality [1-3]. DCM results in dilation of the cardiac chambers and decreased systolic function, often progressing to congestive heart failure, arrhythmias, and sudden death. While historically considered a predominantly inherited disease common to specific breeds such as the Doberman pinscher [4], Great Dane [5], and Irish wolfhound [6], recent concerns have arisen due to anecdotal reports of an increased number of atypical breeds (those breeds without a known hereditary predisposition) developing DCM phenotype [7-9]. Despite the concerns for increased case numbers, the actual incidence of DCM diagnosed by veterinary cardiologists in the United States is poorly understood, and few historical incidence studies exist [2, 10]. The Veterinary Medical Data Base reported a DCM incidence rate of 0.5% among all dogs from 1986-1991 as reported by veterinary referral hospitals [2]. More recently, a DCM incidence rate of 0.4% was reported among all dogs evaluated at a US veterinary teaching hospital from 1995-2010 [10]. While these studies are helpful to understand overall incidence of DCM, they did not report annual incidence rates of DCM over time.

The question of DCM incidence over time is particularly interesting, given recent reports in the veterinary community of a proposed link between certain diets and DCM. In some cases of DCM diagnoses, the dogs were fed foods that are grain-free and/or high in legumes, which may be produced by small companies [7]. Furthermore, a subset of dogs had improved cardiac function on recheck echocardiograms, after being treated with a combination of medical therapy specific to their disease, taurine and carnitine supplementation, and diet change [8,9]. Additional concerns for

an increase in the number of cases of DCM, specifically in atypical breeds, were raised [9]. However, at this time, many questions remain about the role of certain diets in the development of DCM and prospective controlled studies are lacking.

To date, the annual incidence of DCM diagnosed by veterinary cardiologists across the United States has not been reported and no objective data are currently available to evaluate the proportion of different breeds diagnosed with DCM over time. Here, we show the total annual incidence of DCM over the past two decades, as reported by 14 veterinary cardiology services across the United States. Furthermore, our data reveals annual breed distribution of DCM cases from three cardiology services, and annual age distribution from one service. Finally, we report the annual sales of grain-free dog foods over the past decade and discuss the association between grain-free diets and DCM in dogs, as well as alternative hypotheses for the development of DCM phenotype.

Materials and Methods

Data Collection

This study represents a retrospective survey of the incidence of DCM diagnosed by veterinary cardiologists from 2000-2019. Thirty-six veterinary referral hospitals with board-certified or residency-trained veterinary cardiologists were contacted to represent all geographic areas throughout the United States. These referral hospitals included veterinary teaching hospitals at accredited colleges of veterinary medicine, as well as private veterinary referral practices. Services were provided with a DCM Incidence Survey (Supplemental Fig 1) and asked to report on how DCM was diagnosed in their facility, how the cases provided were searched through their

databases, number of cardiologists at the practice, number of cardiology residents at the practice, search terminology used to identify DCM cases, and criteria used to diagnose DCM.

DCM incidence

Services were asked to provide the number of initial (unique) canine cardiology cases seen per year; as well as the number of those cases that had an initial diagnosis of DCM. Recheck appointments of the same patient were excluded. Data were presented in clustered bar charts to provide an overall summary. In addition to this data, one hospital provided all annual initial canine cases (all specialties) presenting to the hospital each year, and these data were analyzed.

Breed distribution

Breed distribution data was provided by three cardiology services (University of Missouri, Columbia, Missouri; Garden State Veterinary Specialists, Tinton Fall, NJ; Red Bank Veterinary Hospitals, Tinton Falls, NJ). A total of 68 breeds were identified from 2004-2019 across the three hospitals. Breeds were divided into six groups: Inherited (breeds with a reported inherited predisposition to DCM) Small breed (< 13.6 kg), Mixed Breeds, Retrievers (Golden Retrievers, Labradors, Chesapeake Bay Retrievers), Other Breeds, and Not Specified. Groups were plotted as stacked plots for ease of visualization, and as scatter plots to evaluate trends over time.

Age distribution

Age distribution data was provided by Red Bank Veterinary Hospital, Tinton Falls, NJ, from 2005-2020. Data were evaluated by comparing the average age of DCM patients upon initial

diagnosis to other canine cardiac patients and other canine patients evaluate by all services. Further, percentage of DCM patients diagnosed at age 0-6 years and 7 + years was evaluated over time.

Pet food sales data

Growth in annual grain-free pet food sales were provided by The Nielsen Company [11] for the years 2011-2019. Additionally, percent market share of dry dog food was provided from 2016-2019 (The Nielson Company, AXCO, Petco, and Petsmart) [11-13]. These data are shared with permission. We also obtained data concerning the total number of dogs in the US over the past decade [14]. Our goal was to estimate the percentage of dogs eating grain-free food in the US in 2011 and 2019. The percentage of dogs in 2011 was estimated using the following equation:

$$\text{\$900,000,000 grain-free sales} / \text{\$50.00 per bag} / \text{12 months} / \text{78,000,000 dogs} = \text{2\%}.$$

This considered the grain-free pet food sales data available from pet-specialty stores only [11]. This equation was repeated for 2019: $\text{\$5,500,000,000 grain-free sales} / \text{\$50.00 per bag} / \text{12 months} / \text{90,000,000 dogs} = \text{10\%}$. Additional data regarding percent of market share of grain free dog food was also considered and resulted in using a range to estimate the percentage of dogs eating grain-free food in 2019. These data are not available for 2011.

Statistical Analysis

The DCM incidence data were analyzed using Statistical Analysis Software (SAS Institute Inc. 2012. SAS/STAT[®] 9.4 User's Guide, Second Edition. Cary, NC: SAS Institute Inc) and expressed as the percent of DCM cases with respect to the number of referrals for each year at

each state site. Response was statistically analyzed through a mixed model random coefficient regression analysis where states were designated as the subjects. A linear overall response was assumed across years. The best fitted regression model assumed a common slope (response trend) allowing for differing intercepts among states. States were evaluated together, and in two groups, based on the trends observed. Significance was set at $p < 0.05$.

Dog breeds were grouped by kind and groups were evaluated using a Poisson regression to analyze breed distributions. The number of dogs in each of the five classes (Inherited, Small Breed, Retrievers, Other, or Mixed Breed) were modelled as a Poisson distributed response variable in a generalized linear model. We modelled the year of each observation as a random effect, controlling for the total number of dogs seen by the cardiology service in each year and the vet hospital (Red Bank, Garden State, or Missouri). Our primary interest was the regression coefficient, its confidence interval, and its p-value. Significance was set at $p < 0.05$. Computations in the breed analysis were performed using the R statistical package.

Results

Of the 36 cardiology services approached, 22 declined to participate because of various reasons such as being unable to search their medical record systems, or not having the resources to do such a search. Fourteen services agreed to provide records and were located in the following geographic areas: East Coast (n=6), Pacific Northwest (n=1), Hawaii (n=1), Midwest (n=5), Southeast (n=1) (Fig 1A). Of the 14 cardiology services that provided data, one provided 19 years of data, two provided 15 years of data, four provided between 8-10 years of data, and the remaining seven services provided five years or less of data (Table 1). Cardiologists reported a variety of

methods in diagnosing DCM, as listed in the DCM Incidence Survey (Supplemental Fig 1); all reported using breed specific reference intervals for left ventricular internal diameter in diastole (LVIDd) and left ventricular internal diameter in systole (LVIDs), fractional shortening (FS) <25%, and breed predisposition as benchmarks for diagnosis. Other parameters were used less frequently for diagnosis of DCM. All database searches included a diagnosis of “DCM”, or “Dilated Cardiomyopathy”, and no services searched specifically for cases with a diagnosis of “Systolic Dysfunction”. Percentage of total initial DCM cases versus the general hospital population were plotted for one hospital (Red Bank – Tinton Falls, NJ) and correspond with previously published data [2,10] (Fig 1B). An upward trend was noted in both percentage of total DCM cases and percentage of total initial cardiology cases vs the general hospital population during this time period, (Figs 1B - C), indicating that the increase in DCM cases corresponded to an overall increase in cardiology caseload. Annual average percentage of DCM was 3.83% (Range 2.41-5.65%, STD +/- 0.77%) (Fig 1D). A mixed model random coefficient regression analysis revealed no upward or downward trend in DCM incidence when all service sites were considered as a whole (Slope = -0.0066, p=0.8492) (Fig 2). One site, Ethos – Hawaii, provided only one year of data and was excluded from the regression analysis. When sites were considered individually, two different trends were appreciated. These sites were grouped based on their negative or positive trends. Seven services (NC, NY, NJ (n = 2), WI, FL, KS) revealed a negative trend that was statistically significant (Slope -0.1115, p = 0.019). Six services (CO, IL, MA, MO, NH, WA) revealed a positive trend that was not statistically significant (Slope 0.0563, p=0.2703) (Supplemental Table I).

Cardiology services from Missouri and New Jersey ($n = 2$) provided additional data on annual breed predisposition (Fig 3). Fig 3A lists all breeds that were diagnosed with DCM phenotype from 2004-2019 from the three different cardiology services and represents how breeds were grouped for analysis. Breed distributions by site are displayed in scatter plots (Fig 3B-D). In all sites, breeds with a known inherited predisposition for DCM comprised the majority of cases diagnosed with DCM annually. Other breeds, including retrievers, mixed breeds, and to a lesser extent, small breeds, were also represented with lower frequencies over the past 15 years. A grouped Poisson regression analysis revealed positive trends for the Small Breed group and Other Breed group over the past 15 years, however these trends were not statistically significant (Small Breed, $p=0.055$, Other Breeds, $p=0.053$). A statistically significant positive trend was discovered in the Mixed Breed group ($p=0.025$), indicating that this group of dogs had an increased trend of DCM diagnoses over the past 15 years. There were no significant trends in the Inherited or Retriever groups (Fig 3D).

One service additionally provided annual age distribution (Red Bank - Tinton Falls, NJ) among DCM patients upon initial diagnosis, compared to all cardiology patients, and all patients annually evaluated by all services at the hospital (Fig 4A-B). An overall upward trend in age was noted among the three groups represented: All Cardiology Patients, DCM Patients, and All Canine Patients, over the past 15 years. DCM patients were consistently younger than other canine cardiology patients, and older than the general canine hospital population at the time of diagnosis. This trend was stable over time, though age of diagnosis increased within each of the three groups over time (Fig 4A). The age of DCM patients was divided into two groups: 0-6 years, and ≥ 7 years, and the trend was plotted over time (Fig 4B). In agreement with Fig 4A, there was a general

upward trend in age at diagnosis of DCM in patients over the last 15 years. Whereas in 2005, 33% of DCM diagnoses were made at 0-6 years of age, and 67% of DCM diagnoses were made at ≥ 7 years of age, the age gap increased in 2020, with 25% diagnosed between 0-6 years of age, and 75% diagnosed at 7 or older, suggesting that dogs with DCM are living longer before diagnosis.

Annual grain-free pet food sales

Data regarding grain-free pet food sales are fragmented, as markets that are not publicly traded are not required to report this information. Furthermore, the percentage of dogs eating grain-free diets is unknown. We obtained two data sets. First, the growth in annual grain-free pet food sales was provided by The Nielsen Company for the years 2011-2019 [11] (Fig 5A). These data included grain-free pet food sales from pet specialty suppliers only from 2011-2015, when sales increased from \$900 million to \$2.7 billion. Beginning in 2016-2019, the sales data additionally reflect brick and mortar food, drug, mass, and convenience stores (along with pet specialty sales), in accordance with the increasing popularity of grain-free diets during this time. Grain-free pet food sales increased to \$5,426,879,686 in 2019. Importantly, not included in these sales data are grain-free pet foods sold by veterinary clinics, farm and feed stores, other stores, or online sales, likely resulting in an underestimate in total grain-free pet food sales from 2011-2019. Additional data from the Nielsen Company, xAOC, and Petco & Petsmart [11-13] providing percent market share of total grain-free pet foods, and grain-free dry dog food were evaluated from 2016 – 2019 (Fig 5B). Total grain-free pet food increased from 21.5% to 29% of the market share from 2016 to 2019, while grain-free dry dog food (the most common dog food type) increased from 31.9% - 43% of all kibble sold during this time (Fig 5B). Using the available data, we estimated that the percentage of US dogs eating grain-free diets was at least 2% in 2011 (based on

the reported dollar sales of pet-specialty stores (\$900 million), and the number of dogs in the US (78 million) [14]. In 2019, considering dollar sales alone (\$5.5 billion) and the total number of dogs (90 million) [14], the percentage of dogs eating grain-free diets was estimated to be approximately 10%. However, when the percent market share of grain-free dry dog food was taken into account (43% in 2019), we estimated that the percentage of dogs eating grain-free diets could be as high 40% in 2019. While a five-fold increase in grain-free pet food sales was noted from 2011-2019, and with this, an increase in the percentage of dogs eating grain-free dog food is estimated, our data do not support a concurrent increase in cases of DCM (Fig 5C). Taken as a whole, these data do not support a correlation between grain-free diet sales and DCM incidence as diagnosed by veterinary cardiologists.

Discussion

Here, we provide a retrospective data set that describes the overall incidence of DCM as diagnosed by 14 veterinary cardiology services across the US over the past two decades. Variation in DCM incidence rates is present at different cardiology services. This is expected, due to multiple regional variables, not limited to: variation in diagnostic methods among cardiologists, different breed distributions across states, regional infectious diseases that may result in myocarditis and other systemic disease, and pet owner demographics. Despite the state-by-state variation in annual DCM incidence, the overall trend does not support a change in DCM incidence, with the average annual incidence rate at 3.83% (Range 2.41-5.65%, STD +/- 0.77%) over the past 19 years. This average is considerably higher than what has been reported previously [2,10], however, our data reflects DCM diagnosed as a proportion of cardiology cases only, rather than

DCM within the whole population. Interestingly, data from one hospital that provided total hospital caseload numbers from 2005-2020 revealed a similar incidence rate to what has been previously reported (Fig 1B), suggesting that the DCM incident rate may be on trend today to what was documented from 1986-1991 [2] and 1995-2010 [10]. Detailed statistical analysis revealed that a group of cardiology services (FL, KS, NC, NJ (2), NY, WI) reported a statistically significant decrease DCM, while other services (CO, IL, MA, MO, NH, WA) reported an upward (but not significant) trend. While these data are interesting, they are difficult to interpret as a particular pattern is not evident to explain these trends. The states, as grouped, do not comprise particular geographical areas of the US, nor is there a clear relationship between them. One explanation for these varying trends is the small data set that is being analyzed. It is possible that if a longer time range were available for analysis among a larger number of services, that the trends would become clearer. Additionally, individual breed popularity by state and regional infectious disease prevalence, as well as other unknown variables, may also play a role in these trends but were not evaluated in this study.

Additionally, we provide data describing the breed distribution of dogs diagnosed with DCM across three hospitals. Evaluation of the available breed predisposition data supports previous studies that describe DCM as a primarily inherited disease, with breeds with a known inherited predisposition comprising the majority of diagnosed DCM each year, in each cardiology practice. Furthermore, retrievers, mixed breed dogs, other large breed dogs, and small breed dogs have historically been diagnosed with DCM, to a lesser extent, for the past 15 years. However, a regression analysis revealed that only the Mixed Breed group had a statistically significant upward trend. Positive trends that were not statistically significant were noted in the Small Breed and

Other Breed groups. These data may support what has been reported by some cardiologists as an increase in atypical breeds developing DCM phenotype [7-9, 15, 16]; however, these data sets are few, and do not support a causative relationship between DCM phenotype and any specific variables. It should also be noted that some dogs in the Mixed Breed group were noted to be mixed with a breed with a known predisposition to DCM (Fig 3), and it is possible that an increased popularity of mixed breed dogs over the past two decades [17,18] has contributed to this upward trend. Additionally, we characterized dogs in the Inherited group as those with a published record of inherited disease. Breeds, such as the Scottish Deerhound, St. Bernard, and Saluki have been reported to be overrepresented [19], however, were placed into the Other Breeds category, as not enough data are available at this time to confirm a hereditary predisposition.

One veterinary hospital provided age distribution data over the past 15 years (2005-2020). These data provide fascinating insight into the age at which dogs are diagnosed with cardiac disease as a whole, compared to the age of the general population of dogs seen by all services at the hospital. In general, across all categories, there is an upward trend to the age at which dogs are evaluated at a specialty and emergency center over the past 15 years, or simply put, our dogs are living healthier for longer. This likely results from several factors including: 1) advancements in medical therapy, 2) increased availability of veterinary care, and 3) increased desire and financial capability of owners to seek advanced medical care for their pets. Compared to the general population, dogs diagnosed with DCM are approximately one year older – this trend continues over 15 years. In contrast, compared to the population of dogs diagnosed with other cardiovascular disease, dogs diagnosed with DCM are approximately one year younger. This is in agreement with past studies that describe the average age of onset of DCM being 6-8 years of

age [20, 21], while the most common cardiac disease diagnosed in the dog, degenerative mitral valve disease [22], tends to have an average onset of 8-10 years of age [22]. It is interesting to consider that, despite the dramatic increase in grain-free pet food sales over the past decade, changes in age distribution over time were not observed. Assuming that dogs of all ages are fed grain-free diets, and that it has been hypothesized that it may take a few as three months to develop nutritional cardiomyopathy secondary to these diets [23], one might expect that the average age of diagnosis of DCM might decrease over time (as younger dogs developed the disease) - if a large enough percentage of dogs were eating grain-free diets and a true correlation existed. Such a trend was not observed with the data, though the actual percentage of dogs eating grain-free diets at this practice during this time period is unknown.

Concern over the relationship between certain diets and DCM has risen over the past few years [7-9, 24-28]. An increase in total DCM cases in Golden retrievers eating grain-free diets has been reported in peer-reviewed literature [7,16,23], though recently an Expression of Concern was reported by the editors [29], leading to further confusion regarding the issue of diet and DCM. Previous studies have also suggested a genetic correlation to taurine deficiency in the golden retriever, irrespective of diet [16, 30]. While our data reveals that retrievers (including goldens, Labradors, and Chesapeake Bay) have been diagnosed with DCM over the past 15 years, an increased incidence was not supported. Further anecdotal reports state cases of DCM increasing in atypical breeds [7-9,24-27], but no measurable data was previously available to support these claims. Our data support a weak upward trend in “atypical breeds,” including mixed breeds (statistically significant trend), and other small and large breeds (not statistically significant) developing DCM over the past 15 years. In addition to external factors such as changes in breed

popularity, infectious disease, and diet, it must be considered that an increase in atypical breeds may simply be a reflection of previously unrecognized heritable cardiomyopathies occurring in the breeds as seen with toy Manchester terriers, standard schnauzers, Welsh springer spaniels, Rhodesian ridgebacks, Dalmatians, and English bulldogs [31-37]

Here, we describe a more than five-fold increase in grain-free pet food sales over the past decade, with no correlating increase in overall DCM incidence. The number of dogs currently eating grain-free diets is unknown, but we estimate it to be between 10-40% of the US dog population (Fig 5C). The massive increase in grain-free diet sales over the past decade means it increasingly likely that dogs will be consuming these foods. Furthermore, grain-free diets are generally considered premium dog foods and are often more expensive than their grain-inclusive counterparts. Therefore, dogs seen by veterinary specialists may be even more likely to be consuming grain-free diets, as they represent a different demographic than the general population. However, an increased likelihood of eating grain-free dog food does not necessarily correlate to increased risk of DCM, and a causative link between grain free diets and DCM has not yet been shown. While anecdotal reports of dogs improving after diet change have been reported as evidence that specific diets were the cause of DCM phenotype [7-9,16, 38] close evaluation of the data reveals multiple variables at play, including initiation of taurine and carnitine supplementation, and medications to treat congestive heart failure and tachyarrhythmias [7-9,16, 28, 38, 39]. All of these factors may play a role in the improvement of cardiac function in cases of DCM phenotype. Furthermore, spontaneous resolution of DCM phenotype had been reported in cases of viral myocarditis, in both humans [40] and dogs [41,42]. These factors must all be considered when trying to determine the underlying primary cause for DCM phenotype.

The authors understand there are many limitations when conducting a retrospective study based on referral case numbers of multiple independent institutions. Some of those include collecting sufficient information from every region of the country, collecting sufficient numbers of years of data from each institution to understand the trend of DCM diagnoses for that particular hospital, and varying criteria for the diagnosis of DCM for each individual referral hospital. More specifically, despite our best efforts, we were able to obtain data from fewer than 10% of board-certified veterinary cardiologists in the US, and while this is the most complete dataset available at this time, it is possible that it does not represent the trends observed by all veterinary cardiologists. The small numbers of animals considered in the breed distribution data are interesting to consider; however, may not give an accurate picture of breed distribution at all cardiology services. Furthermore, the data do not consider risk factors for small cohorts of breeds, which may be excluded from this global study due to small numbers. For example, the golden retriever is overrepresented in all datasets in all years, compared to all other breeds. The authors suggest that this may indicate an, as-of-yet undetermined (though previously suspected) hereditary component to DCM in this particular breed and that golden retrievers may have different dietary requirements regardless of diet [16, 30]. Additionally, the presence of a hereditary component in any of the “atypical breeds” (including mixed breeds) that appear to be overrepresented for DCM should be considered. Finally, the presence of other well-established causes of DCM phenotype, such as myocarditis, hypothyroid disease, or chronic tachycardias should not be ignored when considering the etiology of DCM phenotype. Further data from veterinary cardiologists including all cardiology patients and their detailed diet histories would allow us to assign hazards ratios to these variables.

Limitations notwithstanding, this data comprises the most current data set considering the incidence, age, and breed distributions of canine DCM diagnosed by veterinary cardiologists.

Figure Legends.

Table 1. Annual DCM cases and annual initial cases reported by 14 cardiology services from 2000-2019.

Figure 1. DCM trends in the US.

Panel A. Statewide distribution of cardiology services participating in the survey. Light blue represents services that declined to participate. Dark blue indicates the location of participating services. Grey indicates states that did not have a cardiology service contacted. Panels B and C show scatter plots indicating % DCM cases vs the general hospital population (Panel B), and % total cardiology cases vs general hospital cases (Panel C) at Red Bank, Tinton Falls, NJ from 2005-2020. Percentages in Panel B correspond with previously reported estimates of DCM incidence. Linear regression trend lines are displayed Panel B, $R=0.46347$, Panel C, $R=0.69403$). Panel C shows that the increase in DCM cases noted over time is a function of the increase in total cardiology cases over the time period. Panel D. Bar chart representing overall DCM incidence reported by 10 cardiology services providing 4 or more years of data. Red dotted line denotes average annual incidence among states. Year on year average for all services was 3.83% (Range 2.41-5.65%, STD \pm 0.77%).

Figure 2. Linear regression model

Mixed model random coefficient regression analysis including all services with the exception of Ethos- Hawaii (only one data point). 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.

Figure 3. DCM breed distribution

Panel A. Dogs diagnosed with DCM were divided into 6 groups: 1. Inherited, 2. Mixed Breed, 3. Small Breed <30lb (13.6kg), 4. Other Breeds, 5. Retrievers, and 6. Not Specified.

Panels B-D Annual breed distribution scatter plots from 3 different cardiology services:

University of Missouri (B), Red Bank – New Jersey (C), and Garden State (GS) – New Jersey

(D). 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. Panel E depicts the results of a Poisson linear

regression. The number of dogs in each group was regressed against year, total DCM cases, and

site. Open icon denotes regression coefficient, with lines representing individual confidence

intervals. Mixed breeds (light blue) showed a slightly increased trend, 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 -

0.017). RC= Regression Coefficient.

Figure 4. DCM age distribution

Age distribution of patients from Red Bank Veterinary Hospital (Tinton Falls) from 2005-2020.

Panel A depicts the average age of patients at time of DCM diagnosis (blue triangles), at time of

other cardiovascular diagnosis (green squares), or at the time of presentation for non-cardiac services (black circles). 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. Panel B depicts the percentage of DCM patients that are 6 years or younger (0-6y, grey circles), or 7 years or older (>7y, blue squares) at the time of diagnosis, from 2005-2020. The majority of patients (60% or more) are diagnosed with DCM at age 7 or above. In 2005, 67% of DCM patients were 7 years or older, while 33% were diagnosed at 6 years or younger. In contrast at year end 2019, 80 % of DCM patients were 7 years or older, and 20% were 6 years or younger. These data depict an increased age at initial DCM diagnosis over the past 15 years.

Figure 5. Pet food sales data

Grain-free pet food sales data provided by the Nielsen company, xAOC, and Petco & Petsmart, and used with permission. Panel A 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. Panel B 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. Panel C shows 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:

$$\text{\$900,000,000 grain-free sales} / \text{\$50.00 per bag} / \text{12 months} / \text{78,000,000 dogs} = \text{2\%}.$$

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: $\text{\$5,5000,000,000 grain-free sales} / \text{\$50.00 per bag} / \text{12 months} / \text{90,000,000 dogs} = \text{10\%}.$ These numbers are likely underestimates, as dollar sales do not include all sales of grain-free diets. Additionally, when considering the percent market share of grain-free dry dog food in 2019 (43%), the number of dogs eating grain-free kibble may be as high as 40% of US dogs. In contrast, the average % DCM diagnosed among cardiologists remained stable at 4.1% during this time period.

Supplemental Figure 1.

DCM Incidence Survey provided to veterinary cardiologists.

Supplemental Table 1.

Linear regression data for individual services, all services, and services grouped by trend. n= number of years for which data was provided. Slope and p values are also provided. Statistically significant trends are denoted with an *. Individually, both Garden State (NJ), and SW Florida Vet Specialists had statistically significant negative trends. When sites were grouped with like negative or positive trends, the negative trends group (FL, KS, NC, NY, NJ-GS, NY-RB, WI) was statistically significant, but the positive trends group (CO, IL, MA, NH, WA) was not.

Multiple testing corrections were not performed, but these trends are likely not robust enough to maintain significance. When grouped as a whole, there was no significant trend in % over time.

Acknowledgements:

We would like to thank the following individuals and institutions, without whose assistance, this project would not have been possible:

Dr. Justin Thomason DVM, DACVIM - Cardiology (Kansas State)

Dr. Wendy Arsenault DVM, DACVIM - Cardiology (SW Florida Veterinary Specialists)

Dr. Lynne Nelson DVM, DACVIM - Cardiology (Washington State)

Dr. Ryan Baumwart DVM, DACVIM - Cardiology (Washington State)

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Finally, thank you to Dr. Jim Schwenke and Dr. Charles Danko for assisting with the statistical analysis.

Conflict of Interest Statement:

This study was independently funded by BSM Partners, LLC. BSM Partners LLC is an independent pet food industry consulting firm. The firm provides nutritional, veterinary, product development, quality & food safety, engineering and product innovation services to over xxx pet food companies. The firm also designs and conducts independent research to help improve the lives of pets.

References

- [1] Dutton E, Lopez-Alvarez J. An update on canine cardiomyopathies – is it all in the genes? *J Sm An Prac.* 2018;1-10. doi: 10.1111/jsap.12841.
- [2] Sisson D, Thomas W, Keene B. Primary myocardial disease in the dog. In: A. S. Ettinger, editor, *Textbook of veterinary internal medicine.* WB Saunders, Philadelphia. 2000;p. 874-895.
- [3] Buchanan JW. Prevalence of cardiovascular disorders. In: PR Fox, DD Sisson, NS Moise, *Textbook of canine and feline cardiology.* 2nd ed. WB Saunders, Philadelphia. 1999; p. 4577
- [4] Petric AD, Stabej P, Zemva A. Dilated cardiomyopathy in Doberman Pinschers: Survival, Causes of Death and a Pedigree Review in a Related Line. *J Vet Cardiol.* 2002 May;4(1):17-24. doi: 10.1016/S1760-2734(06)70019-4. PMID: 19081342.
- [5] Meurs KM, Miller MW, Wright NA. Clinical features of dilated cardiomyopathy in Great Danes and results of a pedigree analysis: 17 cases (1990-2000). *J Am Vet Med Assoc* 218:729-732,2001.
- [6] Vollmar AC “The prevalence of cardiomyopathy in the Irish wolfhound: a clinical study of 500 dogs,” *Journal of the American Animal Hospital Association*, vol. 36, no. 2, pp. 125–132, 2000.
- [7] US FDA. FDA Investigation into Potential Link between Certain Diets and Canine Dilated Cardiomyopathy. Jun 27, 2019. Available from: <https://www.fda.gov/animal-veterinary/news-events/fda-investigation-potential-link-between-certain-diets-and-canine-dilated-cardiomyopathy>.
- [8] US FDA. FDA Provides Update on Investigation into Potential Connection Between Certain Diets and Cases of Canine Heart Disease. Feb 19, 2019. Available from: <https://www.fda.gov/animal-veterinary/cvm-updates/fda-provides-update-investigation-potential-connection-between-certain-diets-and-cases-canine-heart>.
- [9] US FDA. Vet-LIRN Update on Investigation into Dilated Cardiomyopathy. Jun 27, 2019. Available from: <https://www.fda.gov/animal-veterinary/science-research/vet-lirn-update-investigation-dilated-cardiomyopathy>.
- [10] Bellumori TP, Famula TR, Bannasch DL, Belanger JM, Oberbauer AM. Prevalence of inherited disorders among mixed-breed and purebred dogs: 27,254 cases (1995-2010). *J Am Vet Med Assoc.* 2013;242(11):1549-1555. doi: 10.2460/javma.242.11.1549.

- [11]. The Nielsen Company. (2020). Grain free dollars sales trend (Report ID RB01) [Nielsen Answers]. NY, NY.
- [12]. Extended all outlet combined (xAOC). (2020). Dollar volume and share, total pet food and dry dog food, regular and grain-free.
- [13]. PetCo & Petsmart (2020). Dollar volume and share, total pet food and dry dog food, regular and grain-free.
- [14] <https://www.statista.com/statistics/198100/dogs-in-the-united-states-since-2000>.
- [15] Weder C. Nutritional cardiomyopathy. 2019. Available from: <https://wilmingtonanimalhealthcare.com/storage/app/media/merged-pdf.pdf>.
- [16] Kaplan JL, Stern JA, Fascetti AJ, Larsen JA, Skolnik H, Peddle GD, et al. Correction: Taurine deficiency and dilated cardiomyopathy in golden retrievers fed commercial diets. PLoS One. 2018; 13(12):e0210233. doi: 10.1371/journal.pone.0210233
- [17] Huffaker C. The meteoric rise of the “oodle” and other cross-breed dogs. Sept 27, 2017. Available from: <https://www.post-gazette.com/local/region/2017/09/25/dogs-goldendoodles-labradoodles-morkies-cocker-spaniels-jack-russels-pets/stories/201709250008>.
- [18] Goldendoodle Association of North America. History of the Goldendoodle. Available from: <https://www.goldendoodleassociation.com/about-the-breed/history-of-the-goldendoodle/>.
- [19] Prevalence of dilated cardiomyopathies in various breed of dogs. Adapted from Sisson DD, Thomas WP. Myocardial diseases. In Ettinger SJ, Feldman EC (eds): Textbook of Veterinary Internal Medicine. 4th ed. Philadelphia, WB Saunders, 1995, p. 995.
- [20] Martin MWS, Stafford Johnson MJ, Celona B. Canine dilated cardiomyopathy: A retrospective study of signalment, presentation, and clinical findings in 369 cases. J Sm Anim Prac. 2009;50(1):23-29. doi: 10.1111/j.1748-5827.2008.00659.x.
- [21] Wess G, Schulze A, Butz V, Simak J, Killich M, Keller LJM, et al. Prevalence of dilated cardiomyopathy in Doberman Pinschers in various age groups. J Vet Intern Med. 2010;24(3):533–8.
- [22] Keene BW, Atkins CE, Bonagura JD, Fox PR, Haggstrom J, Fuentes VL, et al. ACVIM consensus guidelines for the diagnosis and treatment of myxomatous mitral valve disease in dogs. J Vet Intern Med. 2019;33(3):1127-1140.
- [23] Ontiveros ES, Whelchel BD, Yu J, Kaplan JL, Sharpe AN, Fousse SL. Development of plasma and whole blood taurine reference ranges and identification of dietary features associated with taurine deficiency and dilated cardiomyopathy in golden retrievers: A

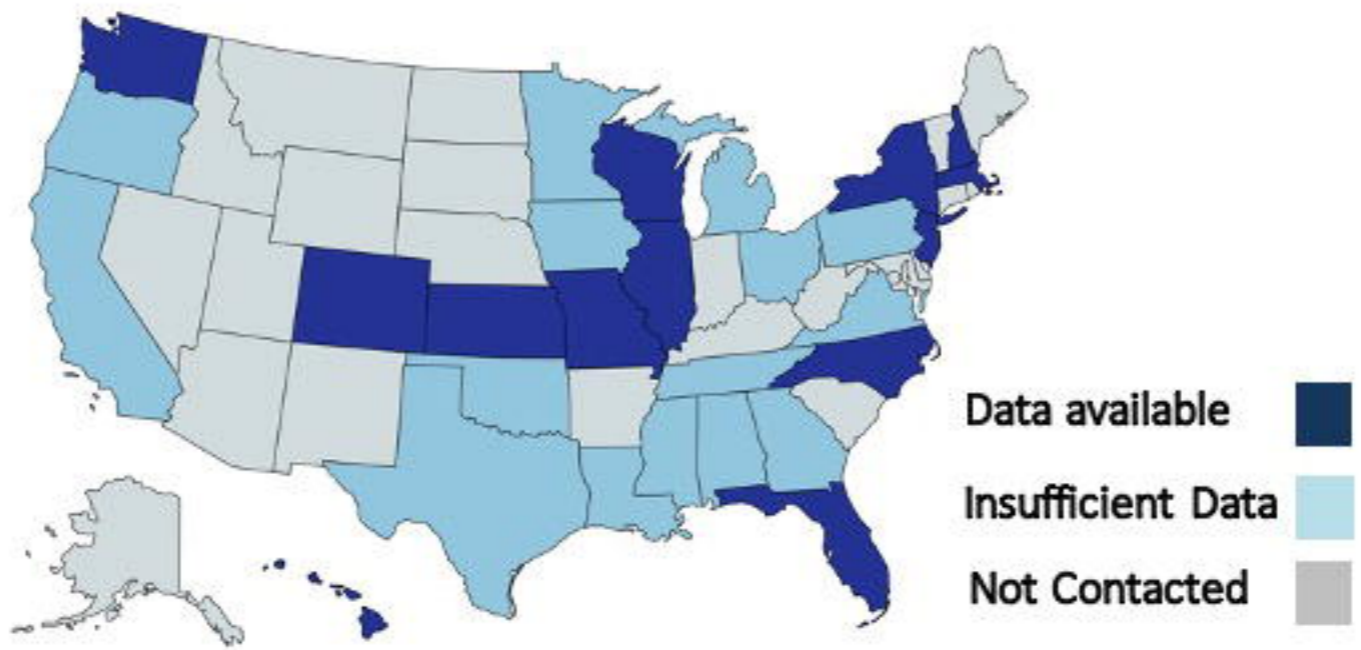
- prospective, observational study. PLoS One. 2020;15(5):e0233206. doi: 10.1371/journal.pone.0233206.
- [24] Freeman LM, Stern JA, Fries R, Adin DB, Rush JE. Diet-associated dilated cardiomyopathy in dogs: What do we know? J Am Vet Med Assoc. 2018; 253(11):1390-1394. doi: 10.2460/javma.253.11.1390.
- [25] Freeman LM. A broken heart: Risk of heart disease in boutique or grain-free diets and exotic ingredients. Jun 4, 2018. Available from: <http://vetnutrition.tufts.edu/2018/06/a-broken-heart-risk-of-heart-disease-in-boutique-or-grain-free-diets-and-exotic-ingredients/>.
- [26] Freeman LM. It's Not Just Grain-Free: An Update on Diet-Associated Dilated Cardiomyopathy. Nov 29, 2018. Available from: <https://vetnutrition.tufts.edu/2018/11/dcm-update/>.
- [27] Freeman LM. Diet-Associated Dilated Cardiomyopathy (DCM): Update, July 2019. July 17, 2019. Available from: <https://vetnutrition.tufts.edu/2019/07/dcmupdate/>.
- [28] Fascetti AJ, Reed JR, Rogers QR, Backus RC. Taurine deficiency in dogs with dilated cardiomyopathy: 12 cases (1997-2001). J Am Vet Med Assoc. 2003;223:1137–1141. doi:10.2460/javma.2003.223.1137.
- [29] The PLOS ONE Editors. Expression of concern: Development of plasma and whole blood taurine reference ranges and identification of dietary features associated with taurine deficiency and dilated cardiomyopathy in Golden Retrievers: A prospective, observational study. PLOS ONE. 2020;15(9):e0239078. doi: 10.1371/journal.pone.0239078.
- [30] Bélanger MC, Ouellet M, Queney G, Moreau M. Taurine-deficient dilated cardiomyopathy in a family of golden retrievers. J Am Anim Hosp Assoc. 2005 Sep-Oct;41(5):284-91. doi: 10.5326/0410284. PMID: 16141179.
- [31] Legge CH, Lopez A, Hanna P, Cote E, Hare E, Martinson SA. Historical characterization of dilated cardiomyopathy in the juvenile toy Manchester terrier. Vet Pathol. 2013;50(6):1043-1052. doi: 10.1177/0300985813480509
- [32] Harmon MW, Leach SB, Lamb KE. Dilated cardiomyopathy in standard Schnauzers: Retrospective study of 15 cases. J Am Anim Hosp Assoc. 2017;51(1):38-44. doi: 10.5326/JAAHA-MS-6506.
- [33] Yost O, Friedenbergs SG, Jetsy SA, Olby NJ, Meurs KM. the R9H phospholamban mutation is associated with highly penetrant dilated cardiomyopathy and sudden death in a spontaneous canine model. Gene. 2019;697:118-122. doi: 10.1016/j.gene.2019.02.022.

- [34] Meurs KM, Weidman JA, Rosenthal SL, Lahmers KK, Friedenbergs SG. Ventricular arrhythmias in Rhodesian Ridgebacks with a family history of sudden death and results of a pedigree analysis for potential inheritance patterns. *J Am Med Assoc*. 2016;248(10):1135-1138. doi: 10.2460/javma.248.10.1135
- [35] Meurs KM, Friedenbergs SG, Olby NJ, Condit J, Weidman J, Rosenthal S, et al. A QIL1 variant associated with ventricular arrhythmias sudden cardiac death in the juvenile Rhodesian Ridgeback dog. *Genes*. 2019;10(2):168. doi: 10.3390/genes10020168.
- [36] Freeman LM, Michel KE, Brown DJ, et al. Idiopathic dilated cardiomyopathy in Dalmatians: Nine cases (1990-1995). *J Am Vet Med Assoc* 209:1592-1596,1996.
- [37] Cunningham SM, Sweeney JT, MacGregor J, Barton BA, Rush JE. Clinical features of English bulldogs with pressure arrhythmogenic right ventricular cardiomyopathy: 31 cases (2001-2013). *J Am Anim Hosp Assoc*. 2018;54(2):95-102. doi: 10.5326/JAAHA-MS-6550.
- [38] Adin D, DeFrancesco TC, Keene B, Tou S, Meurs K, Atkins C. Echocardiographic phenotype of canine dilated cardiomyopathy differs based on diet type. *J Vet Cardiol*. 2019;21:1-9. doi: 10.1016/j.jvc.2018.11.002.
- [39]. Freeman LM, Rush JE, Cahalane AK, Kaplan PM, Markwell PJ. Evaluation of dietary patterns in dogs with cardiac disease. *J. Am. Vet. Med. Assoc*. 2003;223:1301–1305. doi:10.2460/javma.2003.223.1301.
- [40]. Cooper LT. Myocarditis. *N Engl J Med*. 2009;360:1526–1538. doi:10.1056/NEJMr0800028.
- [41]. Ford J, McEndaffer L, Renshaw R, Molesan A, Kelly K. Parvovirus infection is associated with myocarditis and myocardial fibrosis in young dogs. *Vet Pathol*. 2017;54:964–971. doi:10.1177/0300985817725387.
- [42]. Santilli RA, Battaia S, Perego M, Tursi M, Grego E, Marzufero C,et al. Bartonella-associated inflammatory cardiomyopathy in a dog. *J Vet Cardiol*. 2017;19:74–81. doi:10.1016/j.jvc.2016.07.005.

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total cardiology referral cases
Cornell/VSC																					
ANNUAL DCM													37	8	35	39	36	15	26	15	211
ANNUAL INITIAL CANINE													416	122	520	500	396	236	604	375	3169
Ethos-Colorado																					
ANNUAL DCM																		7	33	54	94
ANNUAL INITIAL CANINE																		336	802	1325	2463
Ethos-Hawaii																					
ANNUAL DCM																				26	26
ANNUAL INITIAL CANINE																				660	660
Ethos-Illinois																					
ANNUAL DCM																2	1	20	–	32	55
ANNUAL INITIAL CANINE																68	134	354	–	435	991
Ethos-Massachusetts																					
ANNUAL DCM																			16	26	42
ANNUAL INITIAL CANINE																			1298	1248	2546
Ethos-New Hampshire																					
ANNUAL DCM																		6	46	74	126
ANNUAL INITIAL CANINE																		55	483	510	1048
Ethos-Wisconsin																					
ANNUAL DCM											25	22	20	27	28	31	22	23	14	24	236
ANNUAL INITIAL CANINE											235	267	256	312	294	302	319	322	259	260	2826
Garden State NJ																					
ANNUAL DCM									2	9	12	17	7	15	11	10	13	5	0	2	103
ANNUAL INITIAL CANINE									208	844	1021	910	1044	1126	1134	1127	1131	686	487	476	10194
Kansas State																					
ANNUAL DCM																	13	22	15	18	68
ANNUAL INITIAL CANINE																	560	700	750	907	2917
Red Bank NJ																					
ANNUAL DCM						12	22	41	37	38	38	23	46	42	33	35	35	31	40	50	523
ANNUAL INITIAL CANINE						306	595	991	963	888	804	740	789	763	708	731	873	831	1069	1267	12318
SW Florida Vet. Specialists																					
ANNUAL DCM												24	15	24	22	21	27	32	18	22	205
ANNUAL INITIAL CANINE												469	525	612	618	709	813	977	929	779	6431
U. of Missouri																					
ANNUAL DCM					2	5	16	10	11	5	2	6	6	18	19	12	15	21	41	34	223
ANNUAL INITIAL CANINE					34	356	473	448	434	433	366	369	418	450	441	541	613	732	838	993	7939
VSH North Carolina																					
ANNUAL DCM																	4	17	21	20	62
ANNUAL INITIAL CANINE																	54	671	939	992	2656
Washington State																					
ANNUAL DCM	8	14	14	12	13	16	14	10	14	10	19	9	9	14	15	19	23	22	42	53	350
ANNUAL INITIAL CANINE	181	248	435	475	640	576	410	440	450	560	596	715	670	640	580	556	557	699	752	905	11085
																					67243

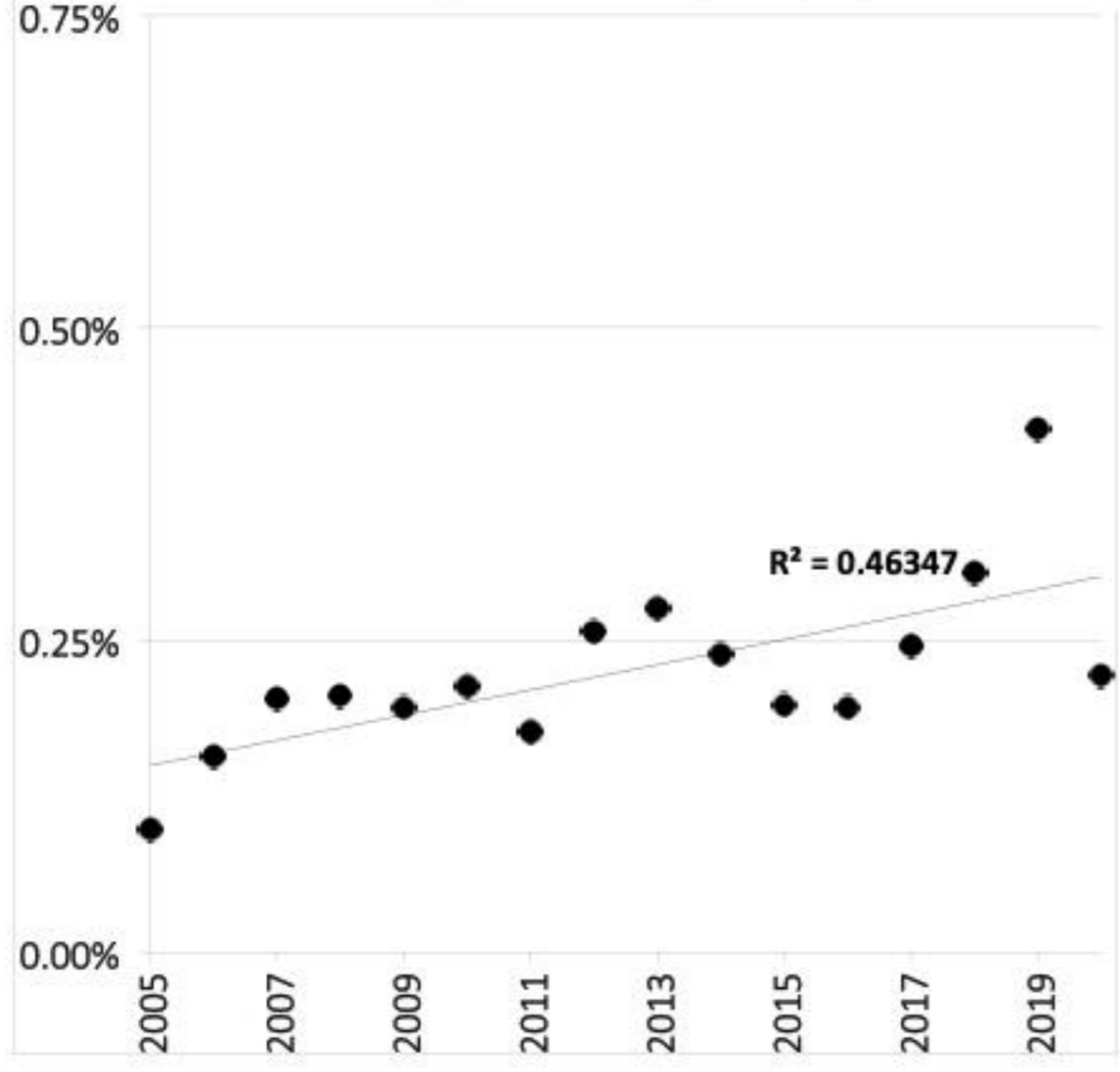
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A



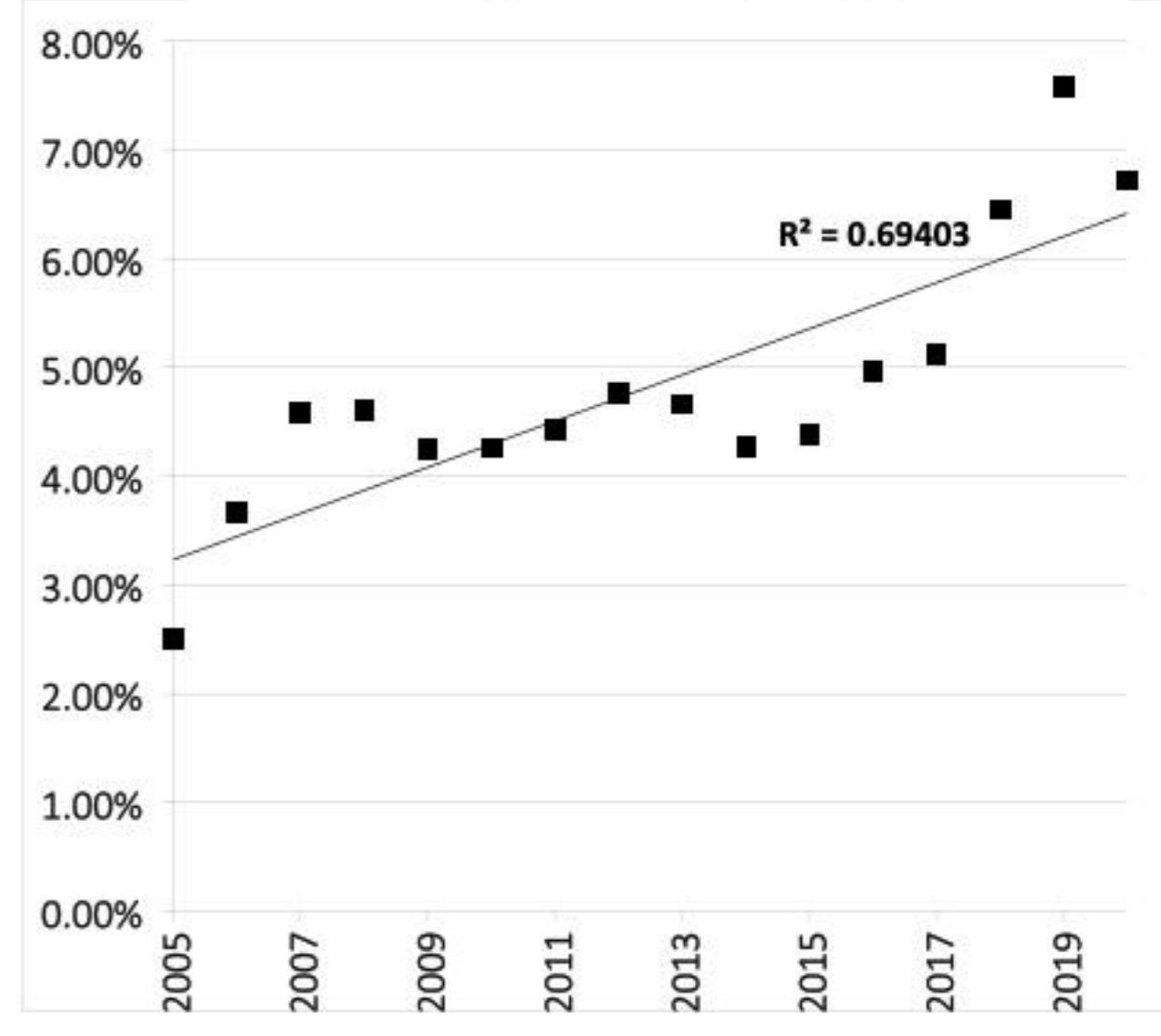
% DCM vs general hospital population

B



% Cardio vs general hospital population

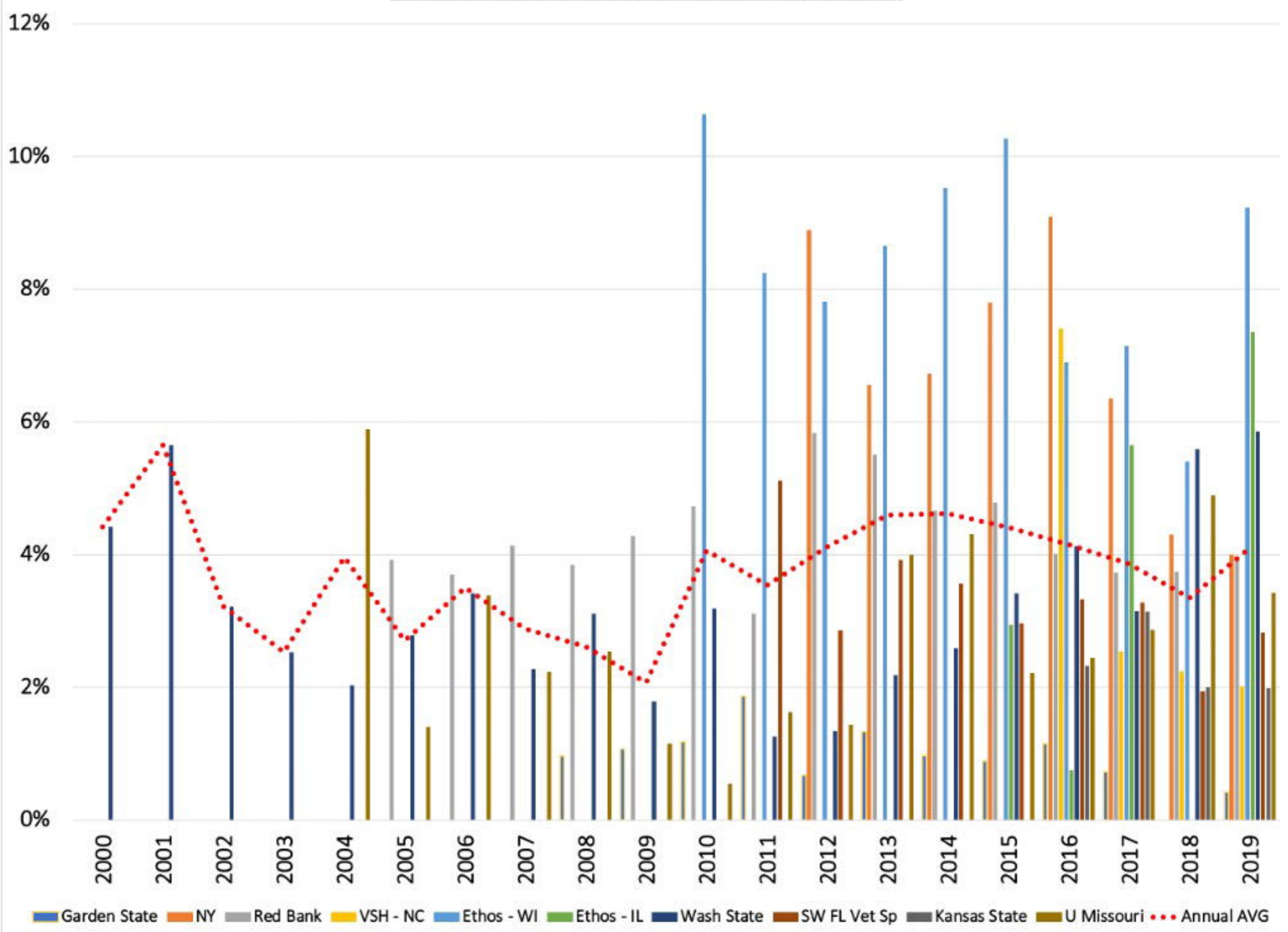
C



D

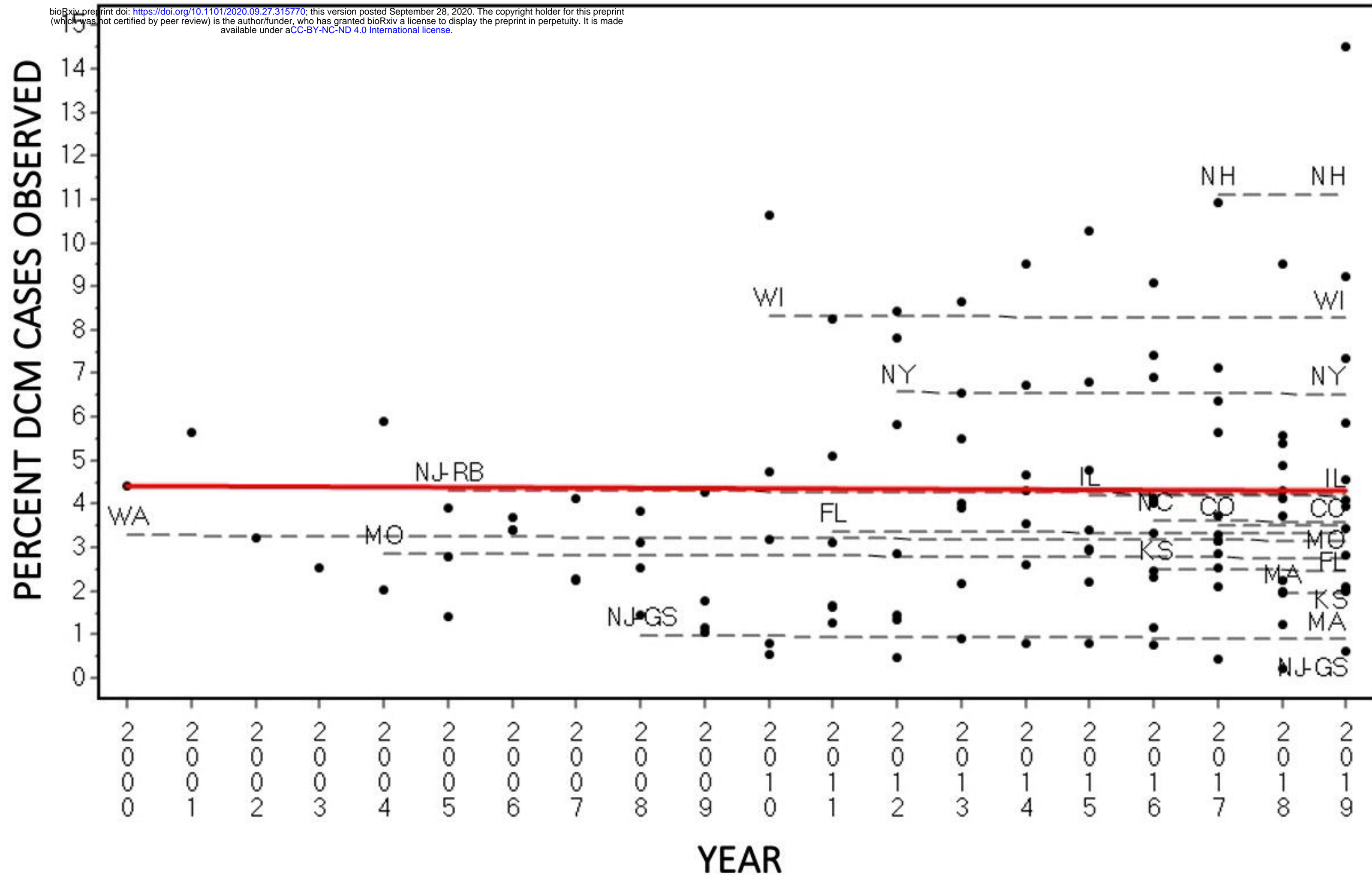
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% DCM diagnosed by veterinary cardiologists



RANDOM COEFFICIENT REGRESSION OF STATE DCM RESPONSE

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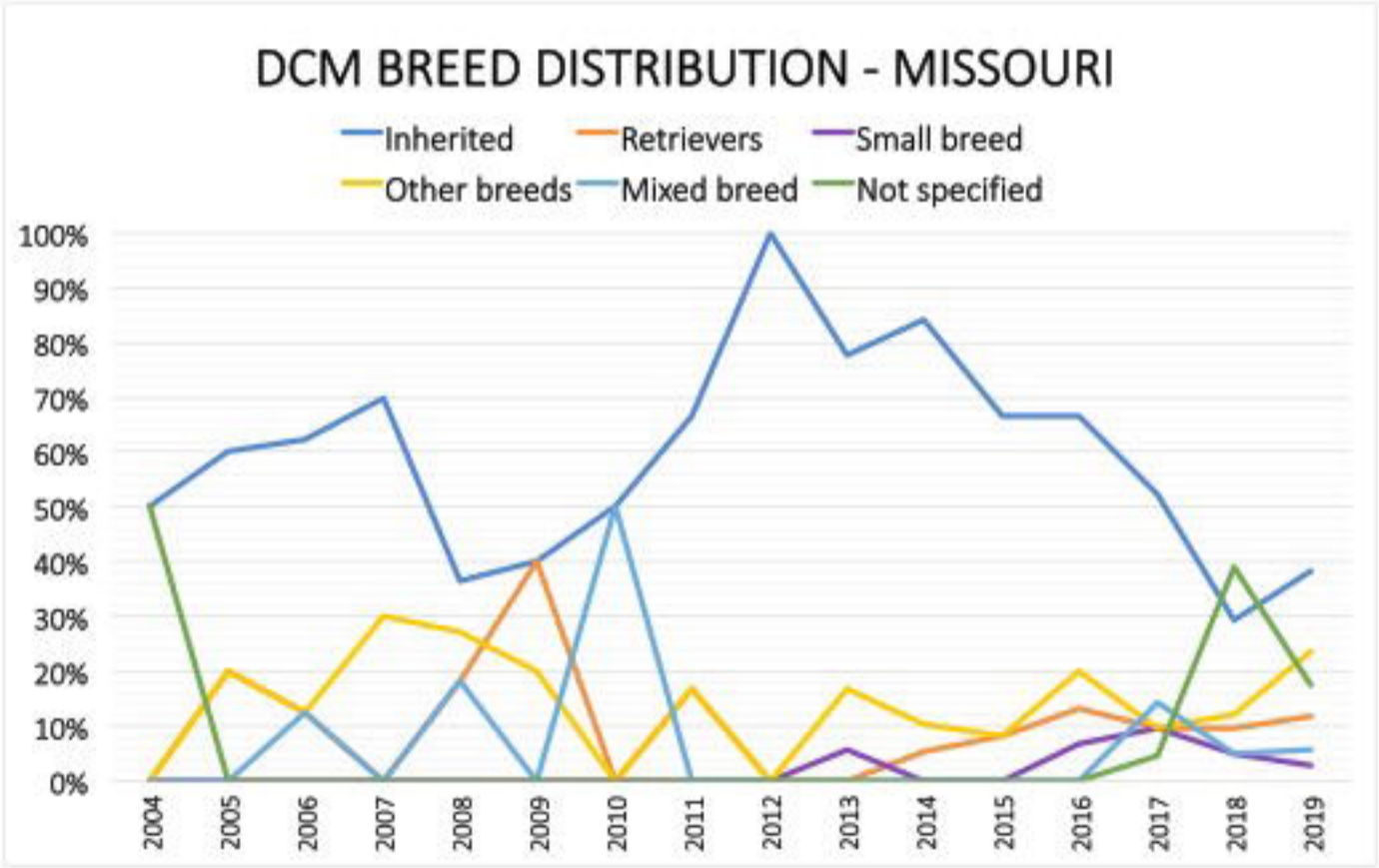


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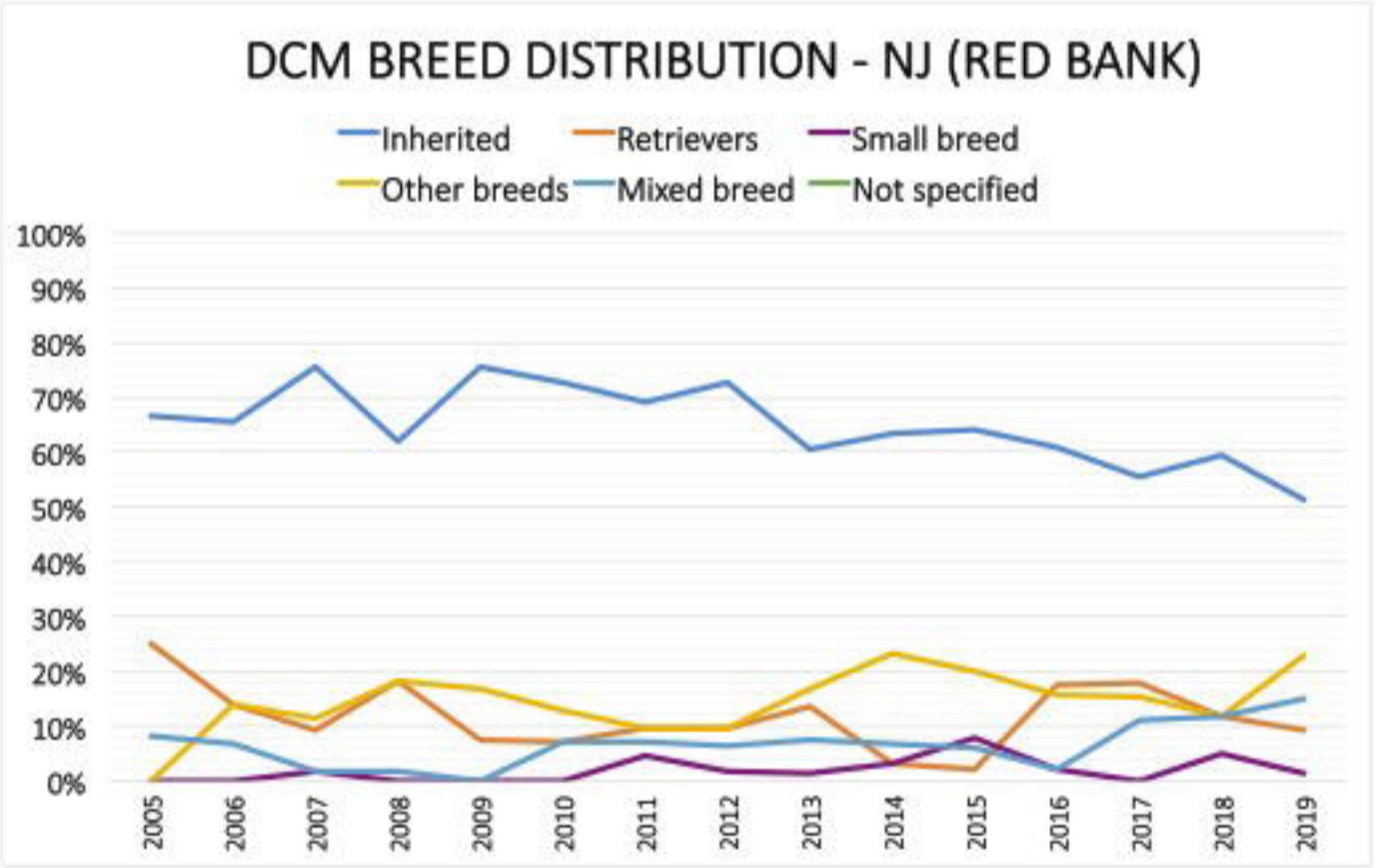
Inherited	Mixed Breed	Small Breed <30lb	Other Breeds	Not Specified
Boxer Cocker Spaniel Dalmation Doberman English Bulldog Great Dane Irish Wolfhound Newfoundland Old Eng Sheepdog Stan. Schnauzer Portuguese WD	Beagle X Boxer X Chow X Doberman X Golden Rtrv X Irish Setter X Hound X Lab X Mastiff X Mix NOS Pitbull X Poodle X Rhod Ridgeback X Rottweiler X Shepherd X Terrier X Whippet X	Boston Terrier Chihuahua X CKCS Cockapoo Coton de Tulear Havanese Irish Terrier Jack Russell Maltese Min Poodle Min Schnauzer Papillon Pomeranian Sheltie Shiba Inu Shih Tzu Whippet Yorkie	Airedale American Bulldog Anatolian Shepherd Australian Cattle Dog Australian Shepherd Basset Hound Beauceron Belgian Malinois Belgian Sheepdog Belgian Tervuren Brittany Spaniel Boerboel Border Collie Borzoi Bouvier des Flanders Bull Terrier Cane Corso Clumber Spaniel Coonhound Corgi (Pembroke) Dogue de Bordeaux English Setter English Spr. Spaniel French Bulldog German Shepherd GSHP Great Pyrenees Greater Swiss MD Irish Setter Korean Jindo Leonburger Mastiff Pit bull Saluki Samoyed Rhod Ridgeback Rottweiler Scottish Deerhound St Bernard Soft Coat Wheat Standard Poodle Weimaraner	
Retrievers				
Chesapeake Bay Golden Labrador				

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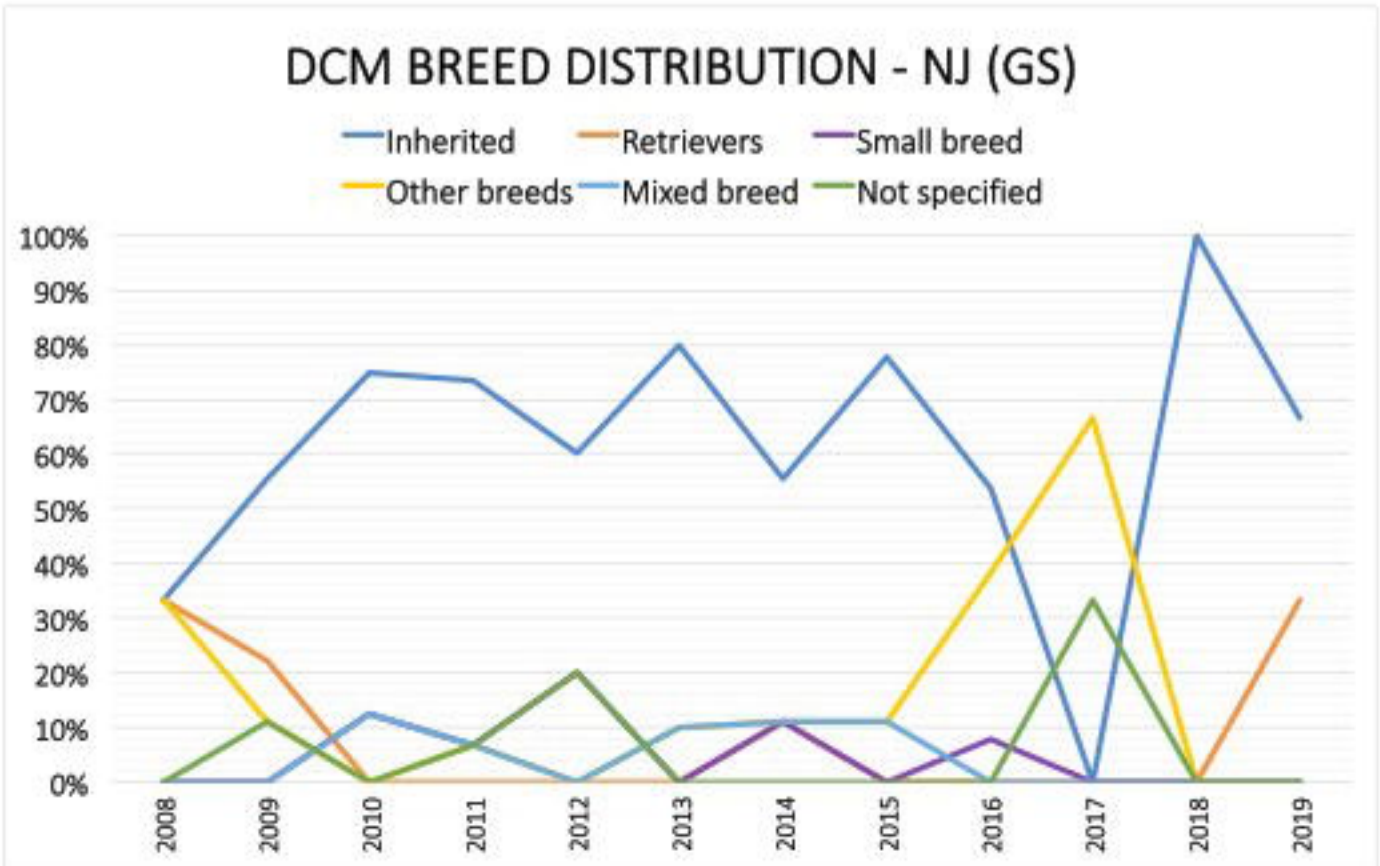
B



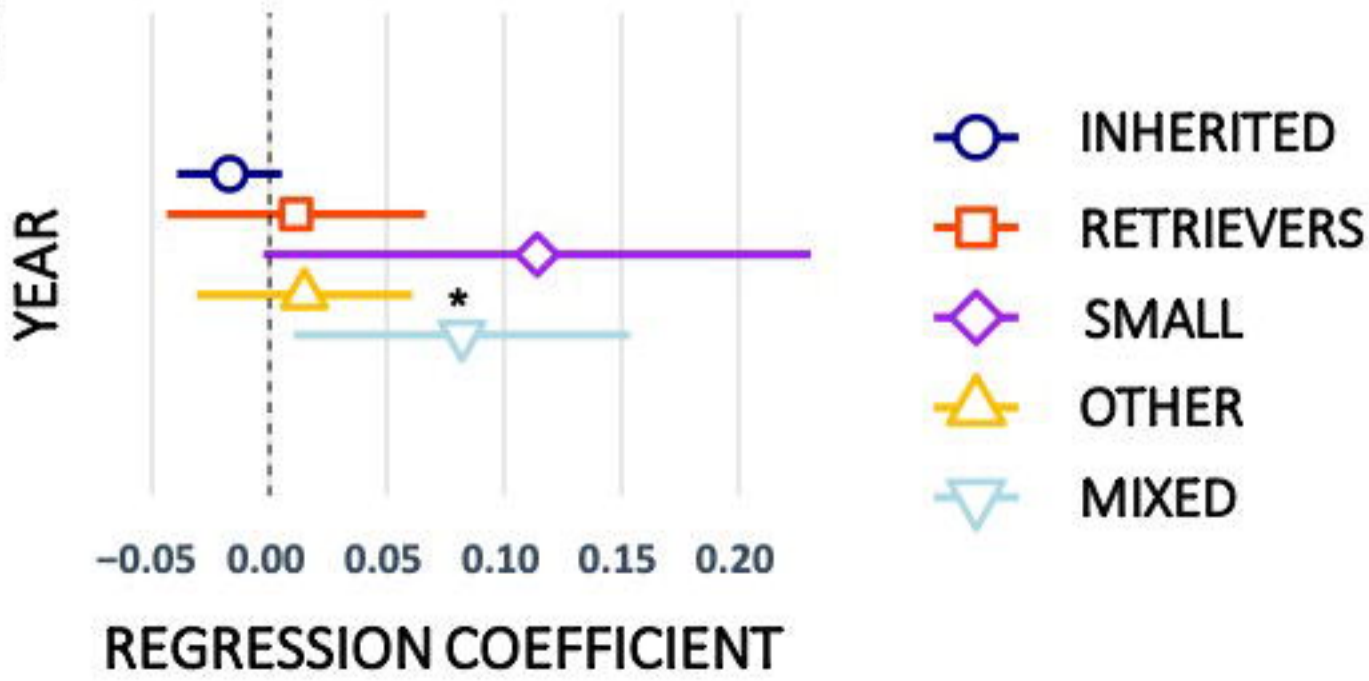
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D

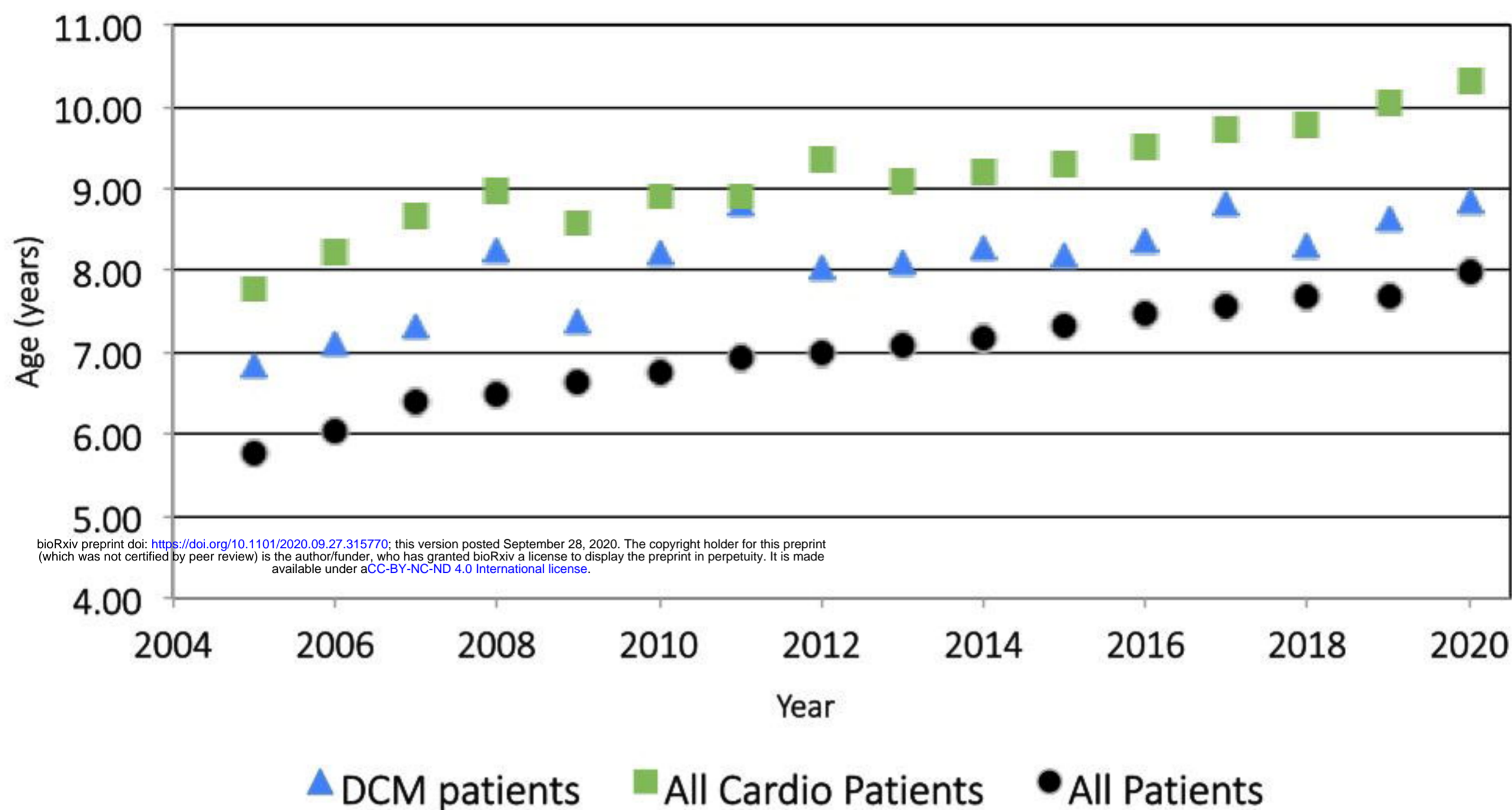


E



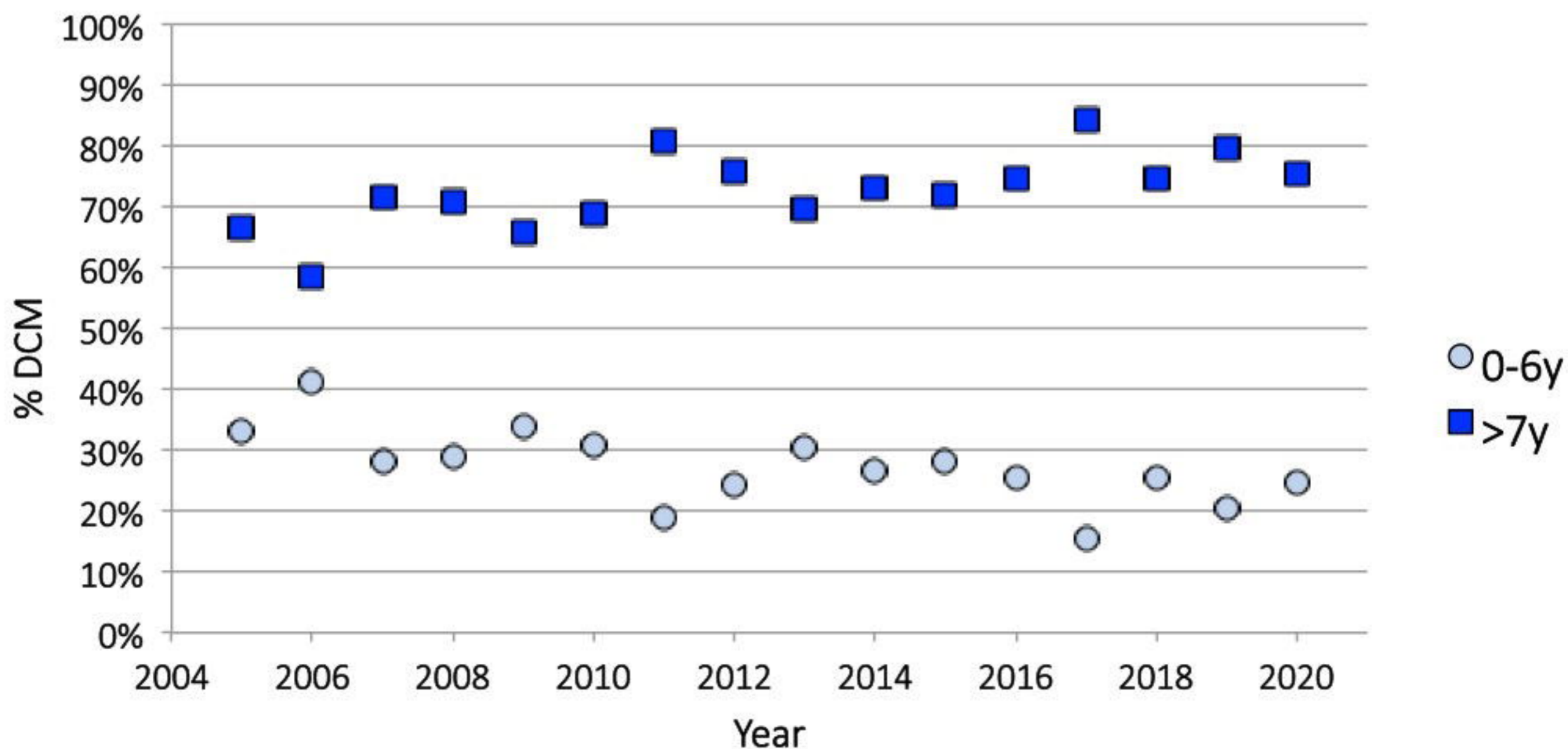
A

Average Age - NJ (Red Bank)



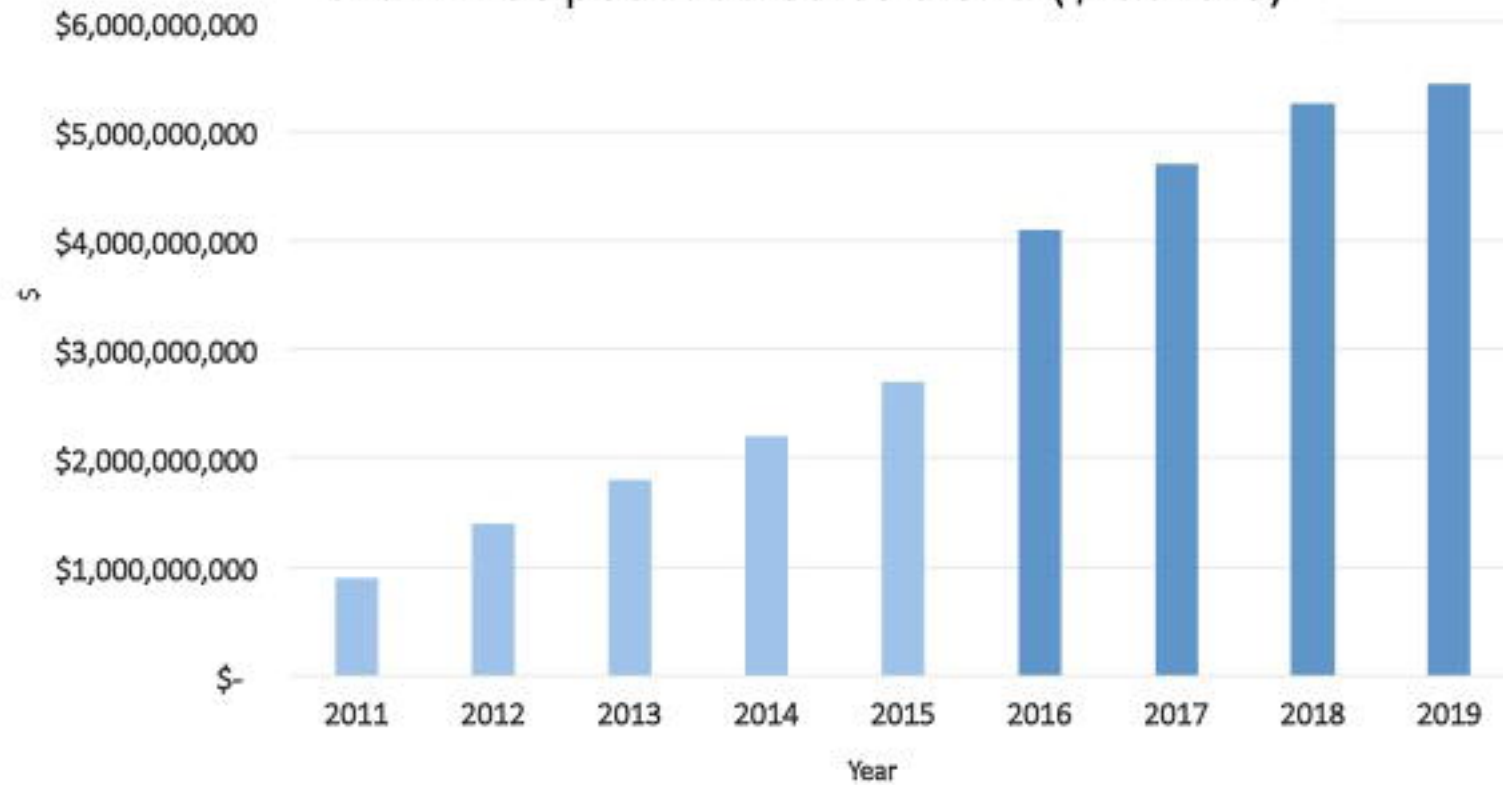
B

Age Group % of Total DCM Patients per Year



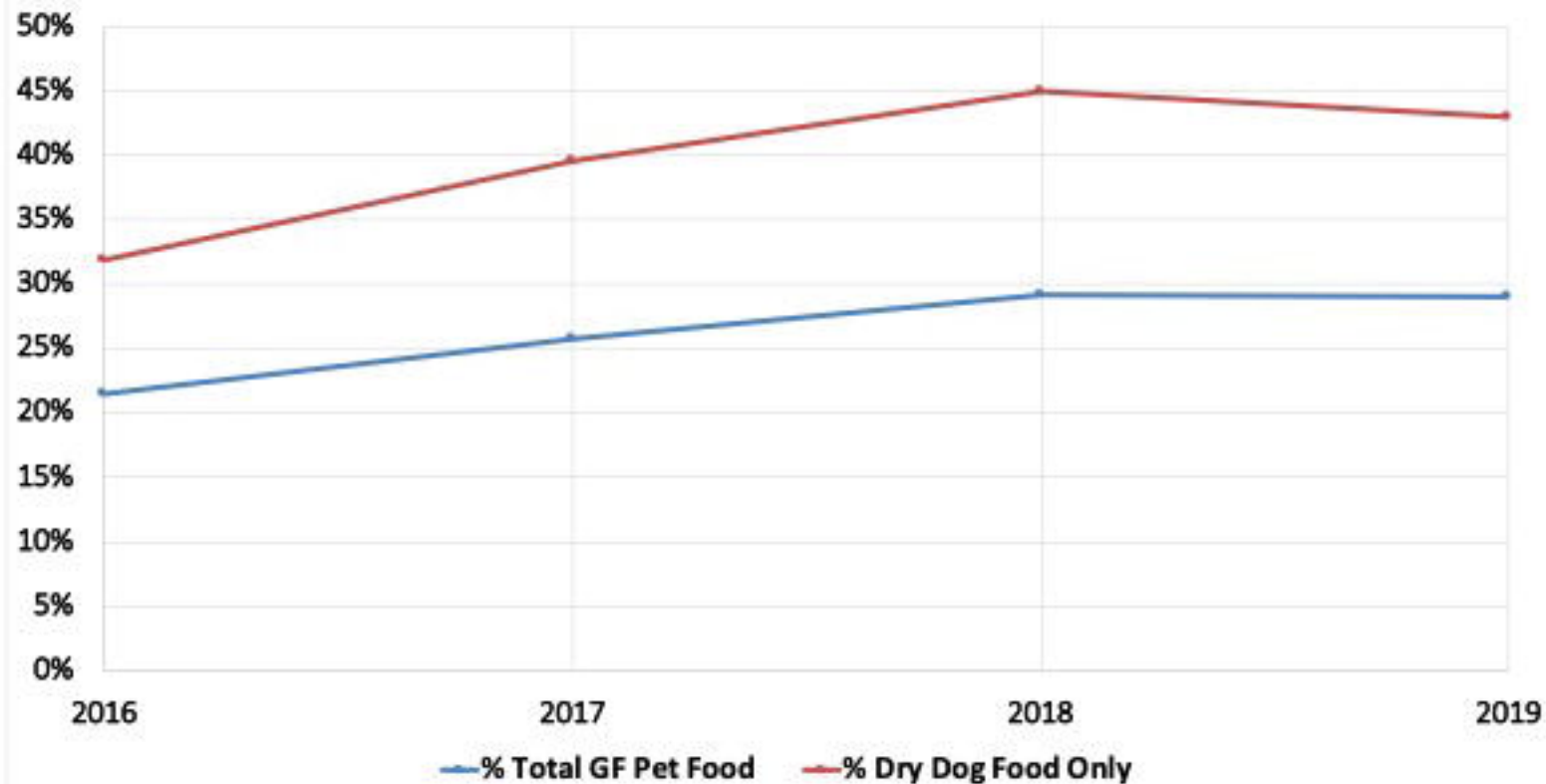
A

Grain free pet food sales trend (\$ dollars)



B

Grain free sales % of Market Share 2016-2019



C

2011 Growth of grain-free dog food 2019



\$ 900 million

🐕 78 million US dogs

🐕 ~ 2% eating grain-free



43% dry dog food sales in 2019



\$ 5.5 billion

🐕 90 million US dogs

🐕 10-40% eating grain-free

