About the size of it: Scaling canine cancer risk



For the third part of a larger analysis of the cancer claims of 1.61 million Nationwide®-insured dogs over six-years, the leading U.S. pet health insurer reviewed data that explored the effect dog size has on the relative risk of cancer, how it differs across body systems, and what effect size and body system has on age of initial cancer claim. *June 2022*

Executive summary

Both clinical experience and academic research have long linked higher rates of some cancers to certain popular breeds, such as splenic tumors in (U.S.) Golden Retrievers[1,2] and bone cancer in Rottweilers.[3,4] But does the size of a dog have a greater or lesser influence on increased relative risk for cancer claims? Do we see higher rates of cancer in large purebred dogs purely as a function of their breed genetics, or is there a primary size-related factor at work as well?

This analysis shows:

- **The larger the dog, the higher the likelihood of a cancer claim.** When graphed, the data show a marked increase in relative risk of cancer claims with each increase in dog size. This "cell phone signal" pattern is maintained across both purebred and mixed-breed dogs, and across most body systems.
- **Mixed-breed dogs present the most useful population to study the effect of size on canine cancer risk.** Analysis in purebred dogs is significantly affected by the genetic factors that appear to be strong drivers of cancer risk among popular breeds.[5]
- **Analyses based on Nationwide pet health data provide evidence-based, clinically actionable cancer insights to veterinary healthcare teams and pet families:**
    - Determining when wait-and-see may not be the best approach – Large and extra-large dogs are at increased risk of bone cancer as early as six years old; knowing what to look for could drive meaningful differences to pet health outcomes.
    - Identifying an evidence-based approach to routine diagnostics – Pet families with medium, large and extra-large dogs who are looking to catch liver cancer early may want to consider routine diagnostics from age eight or younger.
    - Raising the awareness of middle-aged canine cancers – Nationwide data confirm that lymphatic cancers (e.g. lymphoma) are a significantly higher relative risk to dogs in their middle years than other forms of cancer.

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[1] Tamburini BA, Trapp S, Phang TL, Schappa JT, Hunter LE, Modiano JF. Gene expression profiles of sporadic canine hemangiosarcoma are uniquely associated with breed. PLoS ONE. 2009;4(5)e5549
[2] Spangler WL, Culbertson MR. Prevalence, type, and importance of splenic diseases in dogs: 1,480 cases (1985–1989) Journal of the American Veterinary Medical Association. 1992;200(6):829–834.
[3] Rosenberger, J. A., Pablo, N. V., & Crawford, P. C. (2007). Prevalence of and intrinsic risk factors for appendicular osteosarcoma in dogs: 179 cases (1996–2005), Journal of the American Veterinary Medical Association, 231(7), 1076-1080
[4] Karlsson, E.K., Sigurdsson, S., Ivansson, E. et al. Genome-wide analyses implicate 33 loci in heritable dog osteosarcoma, including regulatory variants near CDKN2A/B. Genome Biol 14, R132 (2013). https://doi.org/10.1186/gb-2013-14-12-r132
[5] Dobson J. M. (2013). Breed-predispositions to cancer in pedigree dogs. ISRN veterinary science, 2013, 941275. https://doi.org/10.1155/2013/941275

About the size of it: Scaling canine cancer risk

In 2021, Nationwide's pet insurance division created a dedicated Pet Health Analytics and Insights Team comprised of veterinarians, data scientists, and veterinary communications specialists working in collaboration with Nationwide actuaries, analytics experts, and technology partners. The goal: providing pet owners, veterinary healthcare teams and the veterinary industry with information that contributes to informed, data-driven decisions for the care of companion animals.

In this third study in the series, Nationwide's veterinary insights team analyzed the policy and claims data for more than 1.6 million Nationwide-insured dogs over a six-year period (2015-2021), looking at relative risk for cancer claims by dog size and then digging into those data by affected body system and age of initial cancer claim. For this study, after an initial view that compares relative risks of cancer by size in purebred and mixed breed populations, the focus turns primarily to mixed breed dogs. The rationale behind focusing on the more genetically diverse mixed breed population is that it aims to decouple size-related drivers of canine cancer risk, and those that may be driven by purebred genetics.

There are two previous white papers in this series on cancer claims:

- **"Oodles of Doodles: Popularity and Health,"** on the popularity of poodle crosses and their lower rates of cancer claims compared to their contributing breeds – Poodles, Golden Retriever and Labrador Retrievers.
- **"Diversity of Risk: Purebred Dogs and Cancer,"** on the relative risk of claims for common cancers in popular purebred dogs.

Both studies and all future analyses are available at the Nationwide Pet website, address below. An expanded explanation of methodology of the three analyses of cancer claims is also available at the same location. These studies and others in process are part of a larger effort by Nationwide in pioneering positive change in veterinary medicine, in part through greater use of "big data" by industry players, shared for the benefit of all.

www.petinsurance.com/petdata

About the size of it – how does Nationwide determine dog size?

Size is determined for purebreds based on published breed standards from American Kennel Club or other applicable registries of purebred dogs. For mixed-breed dogs, when pet owners sign up for a Nationwide policy, they are guided through a series of pull-down menus to provide Nationwide with information on the kind of pet to be insured (dog, cat, or avian/exotic, such as rabbits, snakes or parrots). In the case of dogs, the breed or cross is chosen if appropriate, or for mixed-breed dogs, the size. While this information is initially provided by the pet owner, it is verified in the event of an insurance claim by medical review and claims team members.

What are the weight ranges used for dog size?

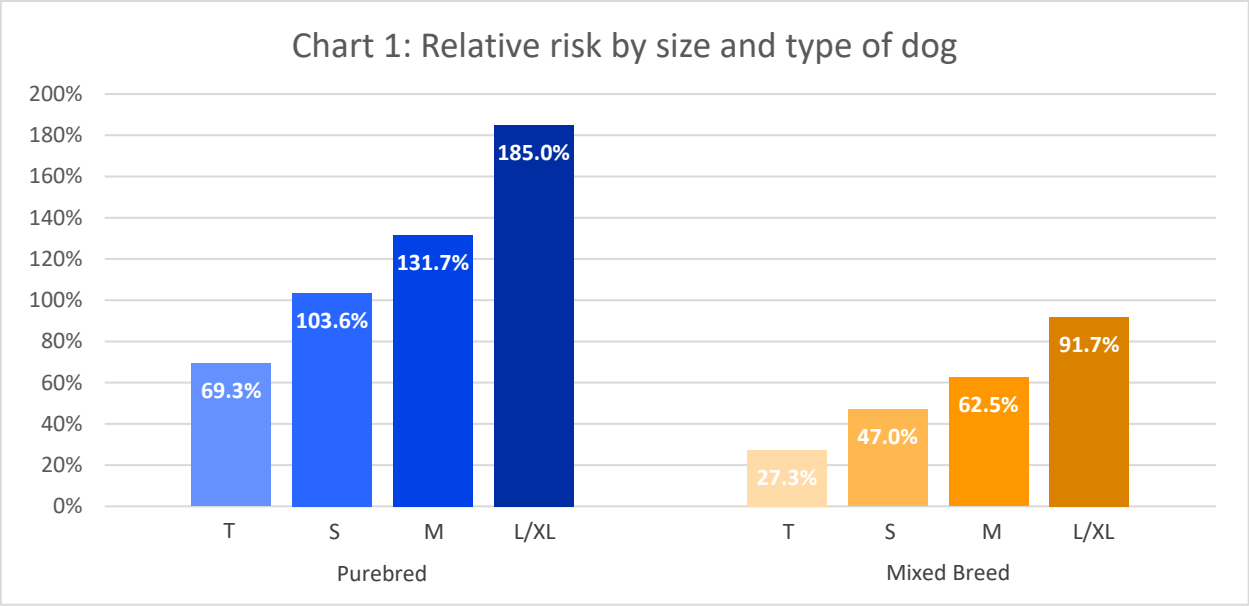
T = toy (10 pounds or less)
S = small (11-30 pounds)
M = medium (31-50 pounds)
L = large (51-110 pounds)
XL = extra-large (111 pounds or more)

Note: for most of this study, large and extra-large dogs were grouped together to ensure a cohort of sufficient size for statistical analysis, leaving four sizes of mixed-breed dogs, each group with tens of thousands of members. When body systems are examined in greater detail, the size groups are further narrowed, combining toy and small dogs into a single group.

About the size of it: Scaling canine cancer risk

The larger the dog, the higher the relative risk

For both mixed breeds and purebreds, the relative risk for a cancer claim increases with the size of a dog. In fact, the trends when represented graphically (see Chart 1) so much resemble the symbol commonly used to indicate a cell phone signal that the Nationwide Pet Health Analytics and Insights Team started calling them simply, “cell phone charts”.



The most striking findings from this chart are that 1) there is a consistent correlation between increased dog size and increased risk of canine cancer across the populations and 2) there is a consistent higher risk to purebred populations compared to the same dog size of mixed breeds (i.e. toy purebreds are at higher risk than toy mixed breeds – this is discussed further in the next section).

A note on relative risk

People read studies with varying levels of comfort when it comes to statistics, so we’ve worked to make the information here as easy to understand as possible for everyone. To that end, we’ve provided the risk ratio (“half as likely,” “three times as likely”) with the combined claims relative risk for all dogs, and, where appropriate, have also provide the relative percentages.

For example, if Dog Size A has a 163.5% risk of having a cancer claim when compared to the mean (average) rate for all dogs, this is equivalent to noting that Dog Size A is 1.63 times more likely to have submitted a claim than the average dog, or that Dog Size A had a 63.5% higher risk of submitting a claim.

About the size of it: Scaling canine cancer risk

Size narrows the gap between purebreds and mixed breeds

The first study in this series, "Oodles of Doodles,"[6] showed compelling differences in cancer risk between purebred and mixed-breed populations. The second study, "Diversity of Risk,"[7] burrowed into how those risks varied across popular dog breeds, with the observed trend that smaller purebreds appeared to have lower relative risk for cancer. This somewhat incidental finding effectively acted as a precursor to this white paper. While the data on the prior page clearly showed that larger dogs are at higher risk, is the difference in relative risk between similarly sized purebred and mixed breed dogs consistent? Could physical size be a consistent predictor of cancer risk independent of breed-specific genetic factors?

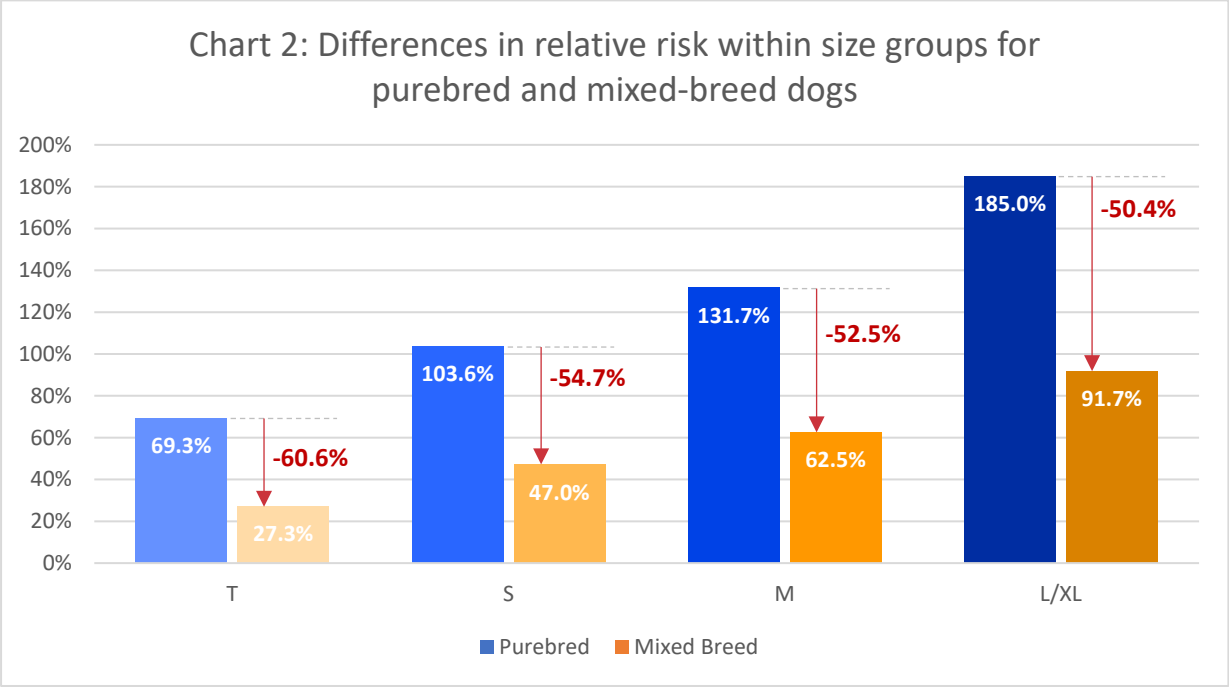


Chart 2 takes the data previously seen in Chart 1 and regroups by dog size. The numbers in red indicate the reduction in relative risk between purebreds and mixed breeds within a dog size category. There is a consistent decrease in the difference between purebred and mixed-breed populations as the analysis moves up from toy (60.6% reduction) to large/extra-large (50.4% reduction), with the reduction in small and medium-sized group risks sitting between.

Said another way, being a toy mixed-breed dog appears to afford more "protection" against cancer than that afforded by the presumed similar genetic advantage of a large mixed breed. This finding is intriguing, and, given the multifactorial origins of cancer, could have myriad causes – some potential areas of explanation are explored in the next section as we look at differences in relative risk across body systems.

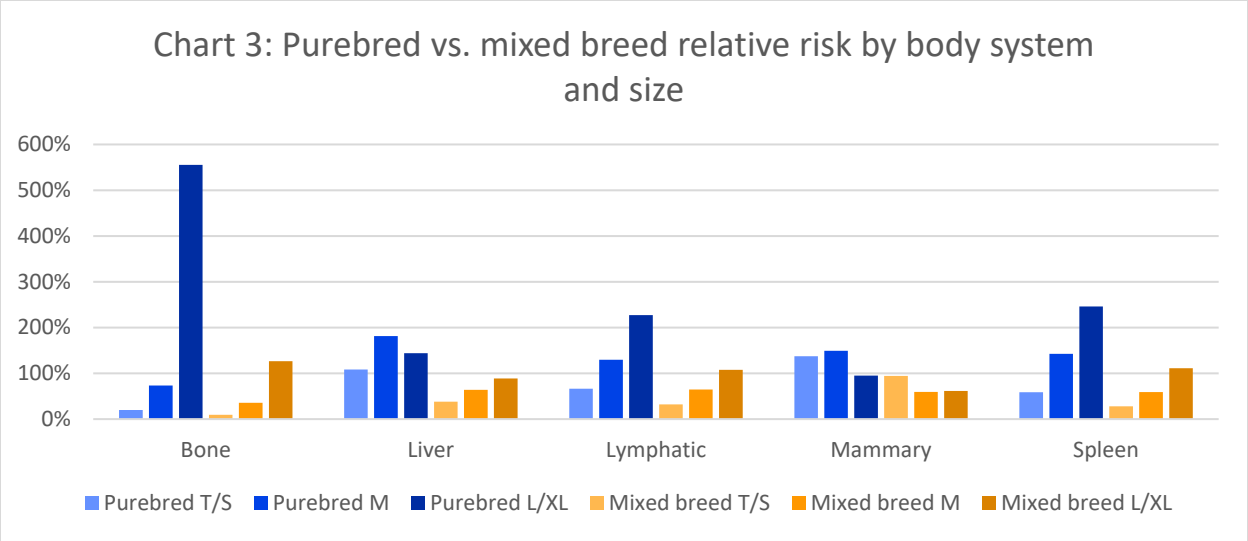
[6] Oodles of Doodles: Popularity and Cancer Claims, (January 2021), PetInsurance.com/petdata
[7] Diversity of Risk: Purebred Dogs and Cancer (March 2021), PetInsurance.com/petdata

About the size of it: Scaling canine cancer risk

Analysis by body system demonstrates challenges in purebred data

Note: Mixed breed dogs make up around 40% of the 1.61 million dogs in the analysis, and the classification of five mixed "breeds" divided by size certainly affords greater statistical simplicity than 300+ pure breeds. However, as the Nationwide Pet Health Analytics and Insights Team delved into cancer by body system and age at initial claim, the team was conscious that, without combining the two smaller classes, they ran the risk of a paucity of significant data in some areas. Therefore, the two smallest size groups, toy and small, were combined in addition to the continued consolidation of the large and extra-large dog data for the remainder of the analysis

When claims are further divided by cancers in specific body systems (see Chart 3), the general trend of larger dogs having a higher relative risk for a cancer claim holds for most systems, as does the trend for purebred dogs being at higher risk. That said, some body system cancers skew even more dramatically towards being "big dog cancer centers" than others, while the differences are not as noteworthy in some body systems, and at least one – mammary cancer – bucks the general trend.



As noted in "Diversity of Risk," specific popular purebreds over index in some kinds of cancer, notably the relative risk of bone cancer in Rottweilers (1009%), liver cancer in Beagles (333%), and splenic cancer in Golden Retrievers (320%). Looking at Chart 3, liver cancer appears to be something of an anomaly in that medium purebreds have the highest relative risk. However, it's noteworthy that a group of popular breeds in this size (Beagle, English Cocker Spaniel, Portuguese Water Dog and Brittany) make up around 22% of that insured population but constitute more than 44% of medium purebreds submitting claims for liver cancer.

This finding demonstrates that any analysis of cancer in purebred dogs is going to be significantly affected by genetic factors that appear to be strong drivers of cancer risk. The proportion of popular breeds represented in the population will drive the output of much of the summary data, as we see in the liver cancer example above. For this reason, this study from this point forward focuses on mixed breed data alone in order to isolate the effect of size as a variable, independent of genetic factors driven by closed breeding populations.

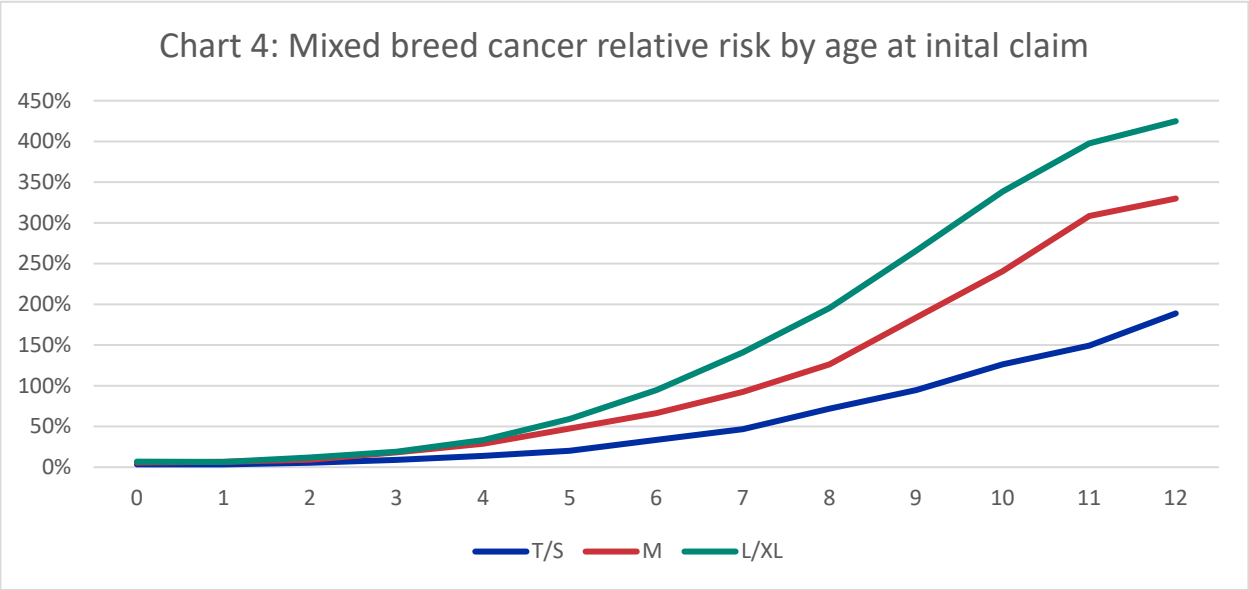
About the size of it: Scaling canine cancer risk

The effect of dog size on relative risk and age of initial cancer claim

Note: Although examination of cancer risk is limited to mixed-breed dogs from here forward, the relative risk values presented are measured against the entire dog population (including purebreds). Any relative risk shown in this study is calculated relative to any other dog, e.g. the risk for a 7-year-old medium mixed breed is calculated relative to all other dogs, purebred or mixed breed, all ages and sizes.

Because mixed breeds have a significantly lower overall risk for cancer in the general population, some of the risk values may seem low. The authors would ask that readers consider the "shape" of the data (i.e. how the data compare to each within the dataset) rather than focus on the absolute values. An option in presenting these data was to recalibrate the relative risk so that it was calculated against only mixed-breed dog data. While this would have presented a more "dramatic" reading of the data, it would also have created discontinuity within the publication and potentially created unnecessary confusion. Additionally, the graph color scheme has been changed to increase the contrast in line graphs.

With the exclusion of purebred relative risk data, mixed-breed dogs are the best model to examine how dog size and age affect the relative risk of canine cancer. Chart 4 shows the relative risk for all cancer claims across mixed breeds through 12 years of age.

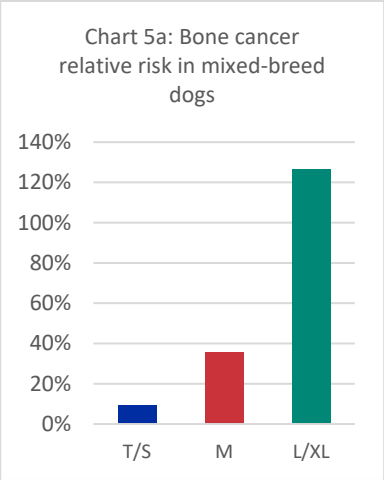


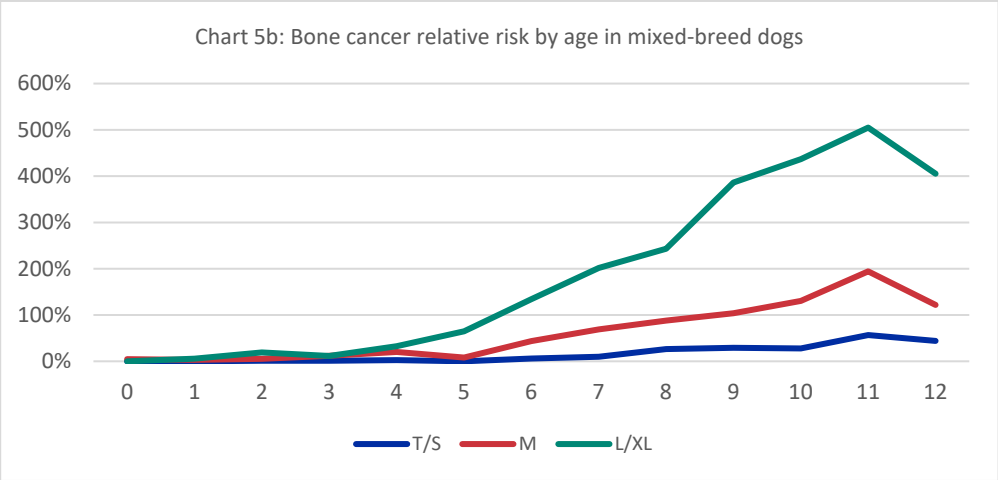
When age is factored in, the same trend holds regarding size, with larger dogs at higher relative risk for a cancer claim and shows that the initial claim comes earlier in the lives of larger dogs. Somewhere between the ages of nine and 10, even toy/small mixed-breed dogs have a higher-than-average relative risk of a cancer claim. For the large/extra-large dogs, though, relative risk for a cancer claim above the mean (i.e. greater than 100%) begins somewhere between the ages of six and seven.

The following five analyses focus on the five body systems shown on the prior page, graphing relative risk by age of onset.

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Bone cancer in mixed-breed dogs





The link between bone cancer and the size of a dog has been well-established[8]; in fact, our "Diversity of Risk" publication on purebred dogs showed large and extra-large dogs at considerably greater relative risk (the largest difference in any of the body systems).

Chart 5a: With purebred dogs removed from the cohort, the same trend remains: large and extra-large mixed breeds are almost four times more likely to have submitted a claim for bone cancer than medium sized mixed breeds, and more than 13 times more likely to have a claim for bone cancer than toy/small mixed-breed dogs.

Chart 5b: Starting at the age of six, large/XL mixed breed dogs already have a 134% relative risk of a bone cancer claim (34% greater risk than other dogs). At 7 years old, this rockets to more than 200%, increasing massively every year until age 11 where relative risk maxes out at more than 500%. This means 11-year-old large/XL mixed breed dogs are five times more likely to submit a claim for bone cancer than the rest of the canine population.

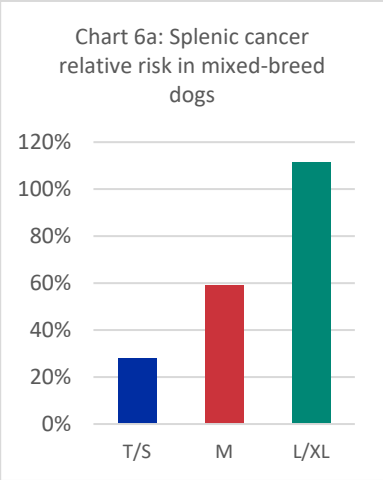
Clinical significance: Perhaps no other finding is more illustrative of the need to educate pet owners about specific risks for individual dogs. As advocates for practicing a spectrum of care, evidence-based insights are pivotal for helping pet families understand when a clinical sign like limping may be 1) initially reasonably managed with basic pet healthcare (e.g pain relievers and rest for a toy/small sized dog) or 2) when a more advanced approach (e.g. x-rays) is strongly recommended from day one for middle-aged large and extra-large dogs.[9,10] The earlier bone cancer is diagnosed, the more treatment options are available, potentially leading to better outcomes.[11]

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[8] Tjalma RA. Canine bone sarcoma: estimation of relative risk as a function of body size. J Natl Cancer Inst 1966;36:1137–1150.
[9] https://news.nationwide.com/spectrum-of-care-education-opportunity/
[10] Fingland, R. B., Stone, L. R., Read, E. K., & Moore, R. M. (2021). Preparing veterinary students for excellence in general practice: building confidence and competence by focusing on spectrum of care, Journal of the American Veterinary Medical Association, 259(5), 463-470. Retrieved Jun 20, 2022, from https://avmajournals.avma.org/view/journals/javma/259/5/javma.259.5.463.xml
[11] Endicott M. Principles of treatment for osteosarcoma. Clin Tech Small Anim Pract. 2003 May;18(2):110-4. doi: 10.1053/svms.2003.36626. PMID: 12831072.

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Splenic cancer in mixed-breed dogs



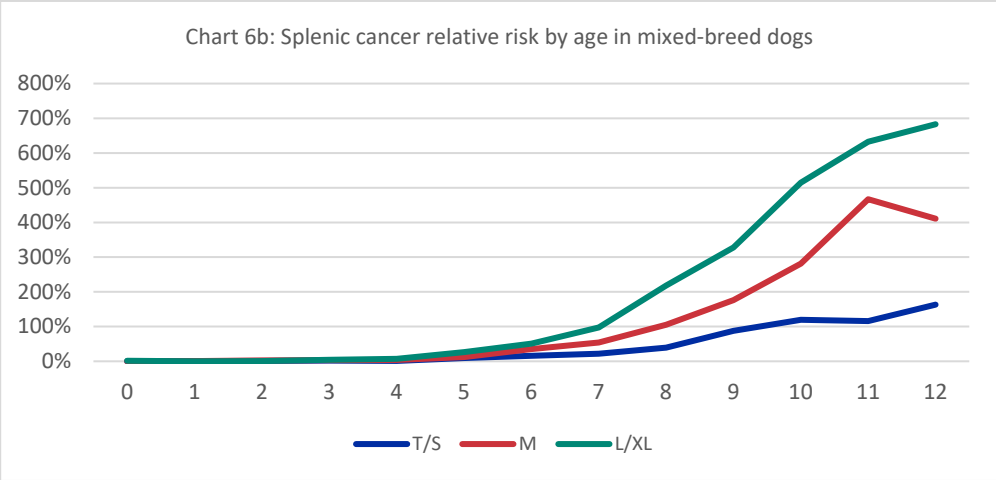


Chart 6a: When looking at data for mixed-breed dogs, claims for splenic cancer highly correlate with size; large and extra-large mixed breeds are almost twice as likely to submit a claim over medium dogs, and almost four times as likely as toy and small mixed breeds.

Chart 6b: Large and extra-large mixed-breed dogs are at greater-than-average risk from around age seven onwards, rising to a peak not dissimilar to bone cancer, where 12-year old large and extra-large mixed breeds are nearly seven times more likely to submit a claim for splenic cancer than the average dog.

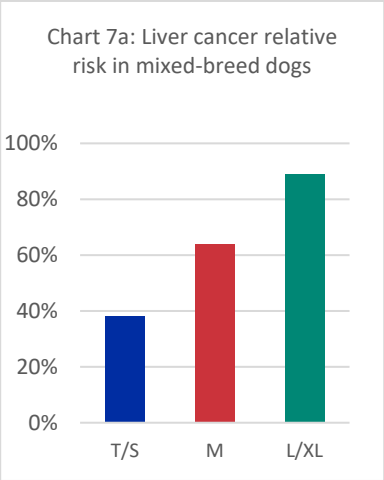
While splenic cancer is far more common in the larger dogs, the baseline rate in the smaller mixed breeds is still significantly higher than it is with bone cancer. Said another way, cancers of the spleen appear to have a strong positive correlation with increase in dog size, but significantly less than is seen with bone cancer.

Clinical significance: Pet families should be made aware of a greater need for observation in older dogs, especially large/extra-large dogs of age 6 and older. Although the most common form of splenic cancer, splenic hemangiosarcoma, is notoriously silent in its development and metastasis, pet families being aware of the clinical signs (e.g. lethargy, decreased appetite, pale gums, distended abdomen, or collapse) may create opportunities for clinical interventions that extend median survival time or improve quality of life, especially when considering breeds with a known predisposition (Golden Retrievers, Labrador Retrievers, and German Shepherd Dogs).[12]

[12] Clifford, C.A., Mackin, A.J. and Henry, C.J. (2000), Treatment of Canine Hemangiosarcoma: 2000 and Beyond. Journal of Veterinary Internal Medicine, 14: 479-485. https://doi.org/10.1111/j.1939-1676.2000.tb02262.x

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Liver cancer in mixed-breed dogs



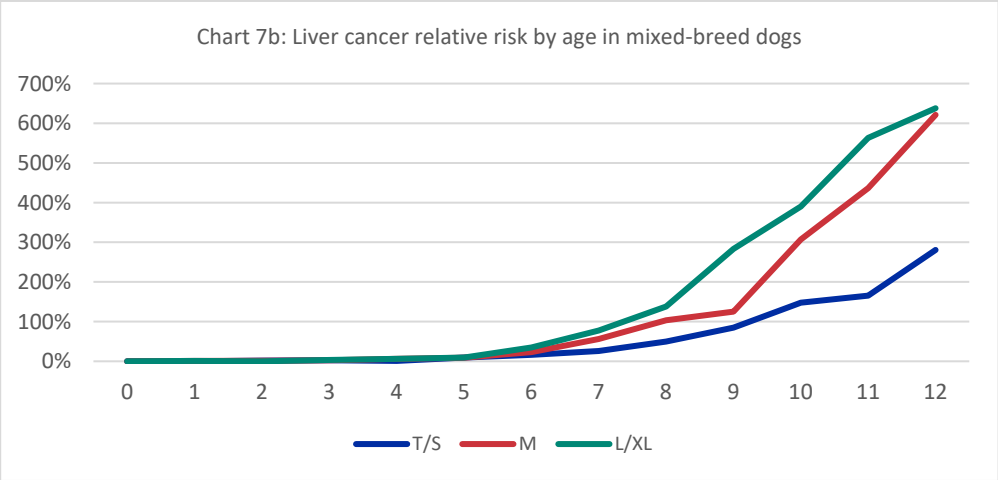


Chart 7a: Despite a lower variation of relative risk across mixed breed sizes than bone or splenic cancers, there is still a clear correlation between size and relative risk – medium dogs were more than 1.6 times more likely to have submitted a claim for liver cancer than their smaller counterparts, and the large dog group was almost 1.4 times more likely to have submitted a claim for liver cancer than the medium mixed breeds.

Chart 7b: In mixed-breed dogs, liver cancer is a disease of older pets, with a steady climb in increased relative risk as dogs age. The relative risk diverges between the smallest dogs and the others at around six years of age, after which medium dogs showing a similar "steepness" of risk as their larger counterparts, but with the medium dog point of upward inflection occurring around two years later than large and extra-large dogs.

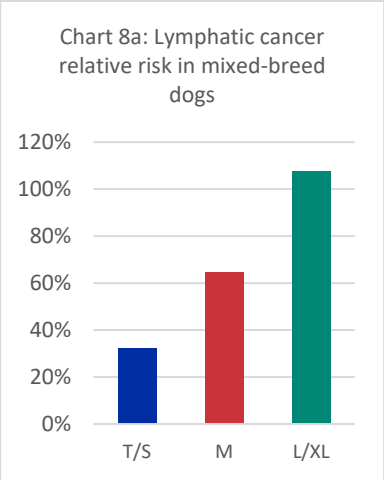
In terms of body systems that follow our established "cell phone" pattern of increase relative risk in larger dogs, while liver cancer seems less affected by size than other common cancers, this familiar pattern is still demonstrated.

Clinical significance: In practice, pet families wishing to practice the most aggressive preventive medicine should be advised to consider senior bloodwork for dogs of all sizes to note emergent concerns that may indicate liver disease in general and cancer in particular. Ultrasounds would further assist in monitoring and diagnosis. [13,14,15]

13 Selmic LE. Hepatobiliary Neoplasia. Vet Clin North Am Small Anim Pract. 2017 May;47(3):725-735. doi: 10.1016/j.cvsm.2016.11.016. Epub 2017 Jan 5. PMID: 28063743.
14 Leela-Arporn R, Ohta H, Tamura M, Nagata N, Sasaoka K, Dermlim A, Nisa K, Morishita K, Sasaki N, Nakamura K, Takagi S, Hosoya K, Takiguchi M. Predictive factors of malignancy in dogs with focal liver lesions using clinical data and ultrasonographic features. J Vet Med Sci. 2019 May 31;81(5):723-729. doi: 10.1292/jvms.18-0673. Epub 2019 Apr 8. PMID: 30956270; PMCID: PMC6541846.
15 Balkman C. Hepatobiliary neoplasia in dogs and cats. Vet Clin North Am Small Anim Pract. 2009 May;39(3):617-25. doi: 10.1016/j.cvsm.2009.01.001. PMID: 19524795.

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Lymphatic cancer in mixed-breed dogs



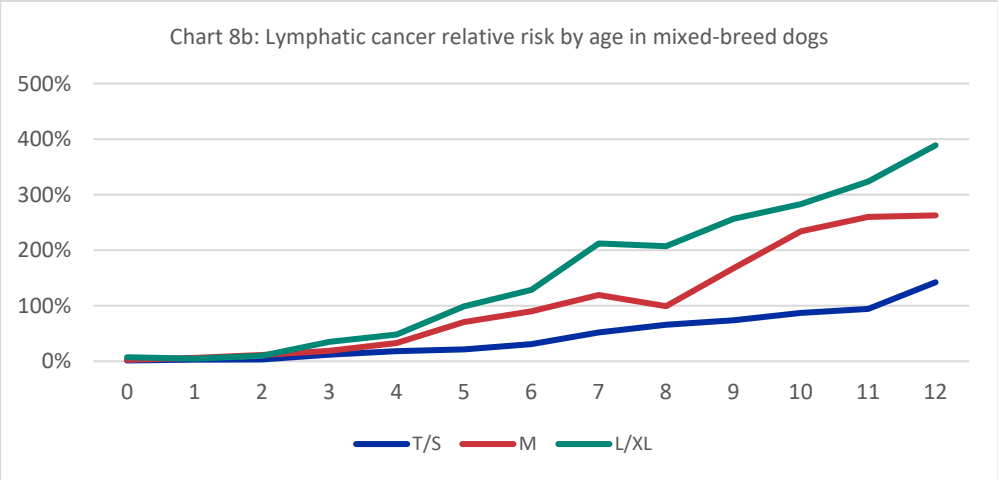


Chart 8a: In terms of the pattern of overall risk (the "shape" of the data), a comparison to splenic cancers is apt, with very similar relative risk profiles across all sizes of mixed breeds.

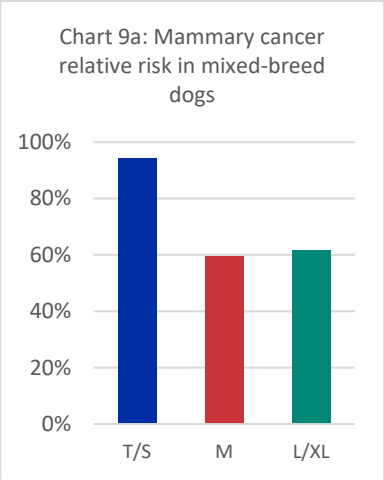
Chart 8b: In contrast to the overall risk being similar to splenic cancers, this age profile chart follows a different pattern. Relative risks for lymphatic cancers in medium, large and extra-large dogs surge much earlier in life, showing an early bump in relative risk at around age seven (for large and extra-large dogs, this relative risk is 212% compared to 97% for splenic cancers at the same age and size). Correspondingly, with this more even spread of lymphatic cancers across adulthood, the maximum value for relative risk among older pets is lower – 389% at age 12 in the group of large dogs, compared to 683% for splenic cancers at the same point.

Clinical significance: The "shape" of these data will likely confirm what veterinary healthcare teams have long experienced: lymphoma, the most common lymphatic cancer, is a significant risk to middle-aged dogs, especially large and extra-large dogs. As a type of cancer that has a range of successful treatment options from basic to advanced, advising pet families of the bump in relative risk rates in middle-aged large and extra-large dogs offers a bright spot for both greater longevity and quality of life.[16]

[16] Zandvliet, M. (2016) Canine lymphoma: a review, Veterinary Quarterly, 36:2, 76-104, DOI: 10.1080/01652176.2016.1152633

About the size of it: Scaling canine cancer risk

Mammary cancer in mixed-breed dogs



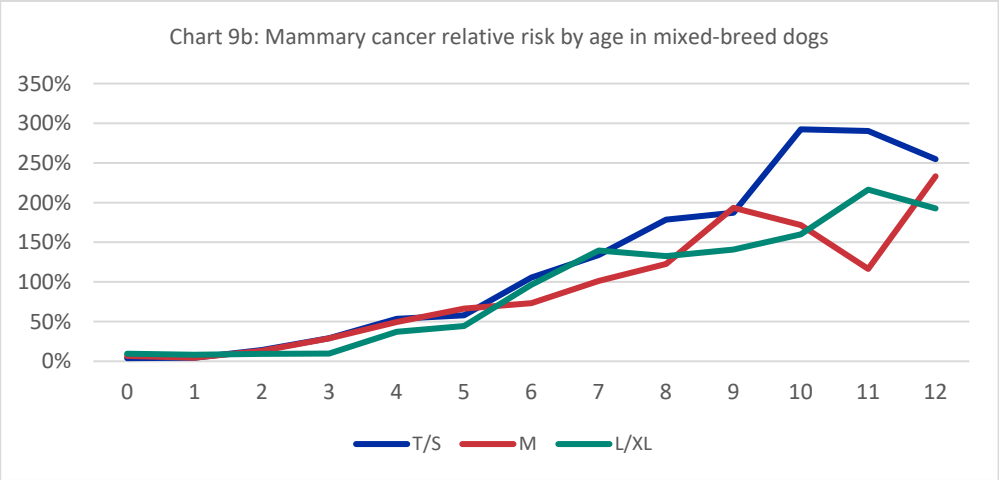


Chart 9a: Mammary cancer appears to be our "exception that proves the rule" when looking at cancer by body system. It should be noted that, while the prevalence of mammary cancers is relatively low (although comparable to bone cancer), the risk data are statistically significant – toy and small breed dogs are at higher risk than their larger counterparts.

Chart 9b: At almost every age, toy and small dogs have a higher relative risk for mammary cancer than all other sizes of dog, although all sizes see a gradual climb up to age nine, diverging more significantly from there.

Since most dogs – and by extension, most insured dogs – in the United States are neutered before full maturity, a question arises: Is there a difference in the average age of spaying in toy dogs vs. all larger dogs? Alternatively, (or perhaps in addition), given toy and small dogs seeming greater resilience to other forms of cancer, is mammary cancer simply the "cancer that gets them" if they live long enough? Preliminary data are inconclusive, but planned future analyses could provide some insights.

Clinical significance: In veterinary practice, assiduous "lumps and bumps" education at age 6 and beyond may be prudent. In the case of small and toy dogs, a more detailed explanation of what to look for is well-advised.

About the size of it: Scaling canine cancer risk

Methodology summary

The cancer claims analysis for this white paper and others in the series was complex, guided by breed experts and veterinarians and conducted/reviewed for adherence to statistical and biostatistical norms. In brief, the in-house Pet Health Analytics and Insights Team looked at all Nationwide-insured dogs, identifying claims activity among 1,612,884 canines over a six-year period (October 2015 to September 2021). The team then identified claims codes relating to cancer diagnosis and treatment and assigned them to one of 23 body systems or a non-specific category. Any policy with a claim submission for a code for the diagnosis or treatment of cancer was used to calculate the relative risk for having submitted a cancer claim.

A complete disclosure and discussion of cancer claims analysis methodology for all cancer studies in this series as well as any possible limitations of our analysis is available as a separate document. [17]

Final note

This is the third of a series of white papers analyzing claims for cancer diagnosis and treatment in dogs, and the first of a larger series of analyses on companion animal health and veterinary industry trends. While most will be conducted by Nationwide's Pet Health Analytics and Insights Team of veterinarians, biostatisticians, actuaries, and science writers, others will be conducted with input from academic partners. As the leading U.S. pet health insurer with more than 1 million pets actively protected, Nationwide believes these studies to be of use to veterinary professionals and pet families alike while helping to advance the use of industry data sources in developing guidance on pet selection and care to the benefit of all.

While these initial studies are limited to cancer, this model of relative risk analysis will act as a foundation for Nationwide to provide evidence-based, clinically actionable tools to veterinary healthcare teams and pet families. Personalizing pet health education will drive more effective preventive care, prolong healthy lifespan, and improve pet health outcomes.

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