**Suppl. Table 1. Antibody panels used for immunophenotyping.**

| Tube | Antibody specificity and fluorochrome |
|---|---|
| **1** | M* IgG1-FITC / M IgG1-PE / M IgG1-Alexa 647 / M IgG1-Alexa 700 / M IgG1-PE-750 / M IgG1-Pacific Blue |
| **2** | CD3-FITC / CD25-PE / CD5-APC / CD8-Alexa 700 / CD4-Pacific Blue |
| **3** | Class II MHC-FITC / CD22-PE / CD21-Alexa 647 |
| **4** | Class II MHC-FITC / CD34-PE / CD5-APC / CD14-PE-Alexa 750 |
| **5** | Class II MHC-FITC / CD18-PE / CD5-APC / CD14 PE-Alexa 750 / CD4-Pacific Blue |
| **6** | CD5-FITC / CD45-PE / CD21-Alexa 647 |

*M = mouse

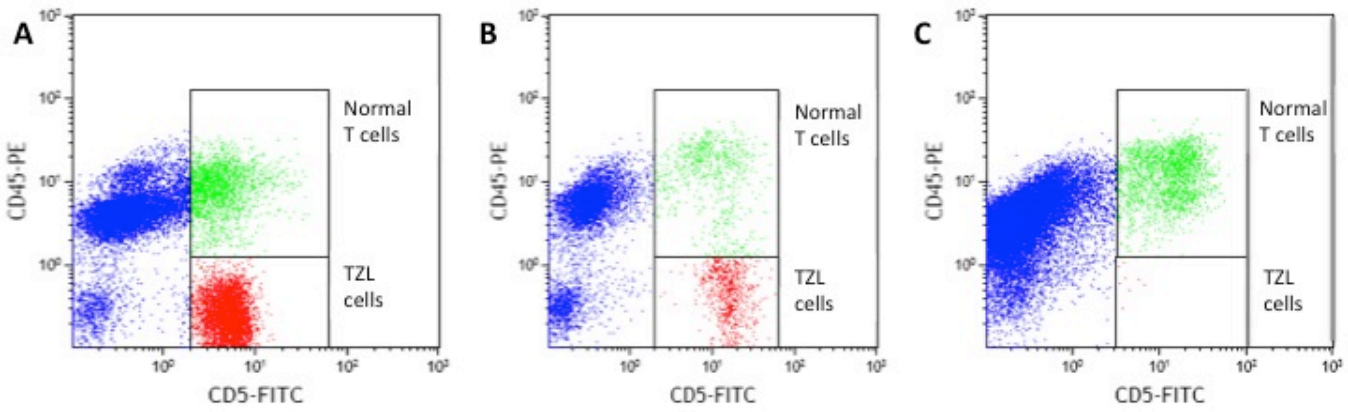
Unless otherwise noted, all antibodies were purchased from Bio-Rad. Clones are as follows: CD45 = YKIX716.13, CD18 = YFC118.3 (human CD18), CD4 = YKIX302.9, CD8 = YCATE 55.9, CD5 = YKIX322.3, CD21 = CA2.1D6, CD22 = RFB4 (human CD22, purchased from AbCam), CD3 = CA17.2A12, CD14 = TUK4 (human), class II MHC = YKIX334.2, CD34 =

**Suppl. Table 2. Modeling results for case vs. control sensitivity analyses.** *Final model* indicates the model reported as our main results (n=140 cases, n=147 controls). *Age sensitivity analysis* removed 20 cases that were <9 years of age (n=120 cases, n=147 controls). *Cancer sensitivity analysis* removed both cases and controls with a history of or concurrent non-lymphoma cancer (n=119 cases, n=111 controls). % change indicates the percent change in the OR estimate compared to the final model.

| | | Final model | | | | Age sensitivity analysis | | | | | Cancer sensitivity analysis | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | OR | (95% CI) | Indiv p-value | Type3 p-value | OR | (95% CI) | Indiv p-value | Type3 p-value | % change | OR | (95% CI) | Indiv p-value | Type3 p-value | % change |
| Age at spay/neuter (vs. Female <1yr) | Female >1yr | 0.34 | (0.16 - 0.74) | 0.007 | | 0.39 | (0.17 - 0.85) | 0.018 | | 12% | 0.39 | (0.17 - 0.90) | 0.028 | | 12% |
| | Male <1yr | 0.62 | (0.3 - 1.3) | 0.206 | | 0.65 | (0.30 - 1.40) | 0.274 | | 5% | 0.74 | (0.32 - 1.70) | 0.474 | | 19% |
| | Male >1yr | 0.93 | (0.4 - 2.16) | 0.862 | | 0.91 | (0.37 - 2.22) | 0.827 | | 2% | 0.84 | (0.33 - 2.11) | 0.704 | | 10% |
| | Missing | 1.44 | (0.46 - 4.46) | 0.530 | 0.031 | 1.72 | (0.55 - 5.42) | 0.352 | 0.054 | 20% | 1.26 | (0.36 - 4.43) | 0.723 | 0.175 | 13% |
| DHPP | As directed (vs. not) | 3.21 | (1.58 - 6.51) | 0.001 | 0.001 | 3.03 | (1.47 - 6.24) | 0.003 | 0.003 | 6% | 3.45 | (1.58 - 7.55) | 0.002 | 0.002 | 8% |
| Bladder infection | Yes (vs. no) | 3.49 | 0.96 - 12.67) | 0.057 | 0.057 | 2.95 | 0.77 - 11.35) | 0.116 | 0.116 | 16% | 2.94 | 0.64 - 13.36) | 0.164 | 0.164 | 16% |
| Mange | Yes (vs. no) | 5.50 | (1.44 - 21.1) | 0.013 | 0.013 | 5.78 | 1.49 - 22.39) | 0.011 | 0.011 | 5% | 11.52 | 1.36 - 97.29) | 0.025 | 0.025 | 109% |
| Eye disease | Yes (vs. no) | 2.25 | (0.97 - 5.22) | 0.059 | 0.059 | 2.49 | (1.06 - 5.88) | 0.037 | 0.037 | 11% | 1.52 | (0.58 - 3.94) | 0.394 | 0.394 | 33% |
| Gastrointestinal disease | Yes (vs. no) | 2.38 | (0.98 - 5.76) | 0.055 | 0.055 | 2.20 | (0.90 - 5.40) | 0.085 | 0.085 | 7% | 3.30 | (1.13 - 9.65) | 0.030 | 0.030 | 39% |
| Hypothyroidism | Yes (vs. no) | 0.25 | (0.1 - 0.66) | 0.005 | 0.005 | 0.27 | (0.10 - 0.74) | 0.011 | 0.011 | 8% | 0.40 | (0.14 - 1.15) | 0.089 | 0.089 | 60% |
| Omega-3 supplements (vs | Yes | 0.29 | (0.13 - 0.63) | 0.002 | 0.007 | 0.27 | (0.12 - 0.62) | 0.002 | | 6% | 0.32 | (0.14 - 0.79) | 0.012 | 0.026 | 12% |
| | Missing | 0.88 | (0.44 - 1.73) | 0.704 | | 0.94 | (0.47 - 1.88) | 0.857 | | 7% | 1.20 | (0.56 - 2.56) | 0.643 | | 37% |

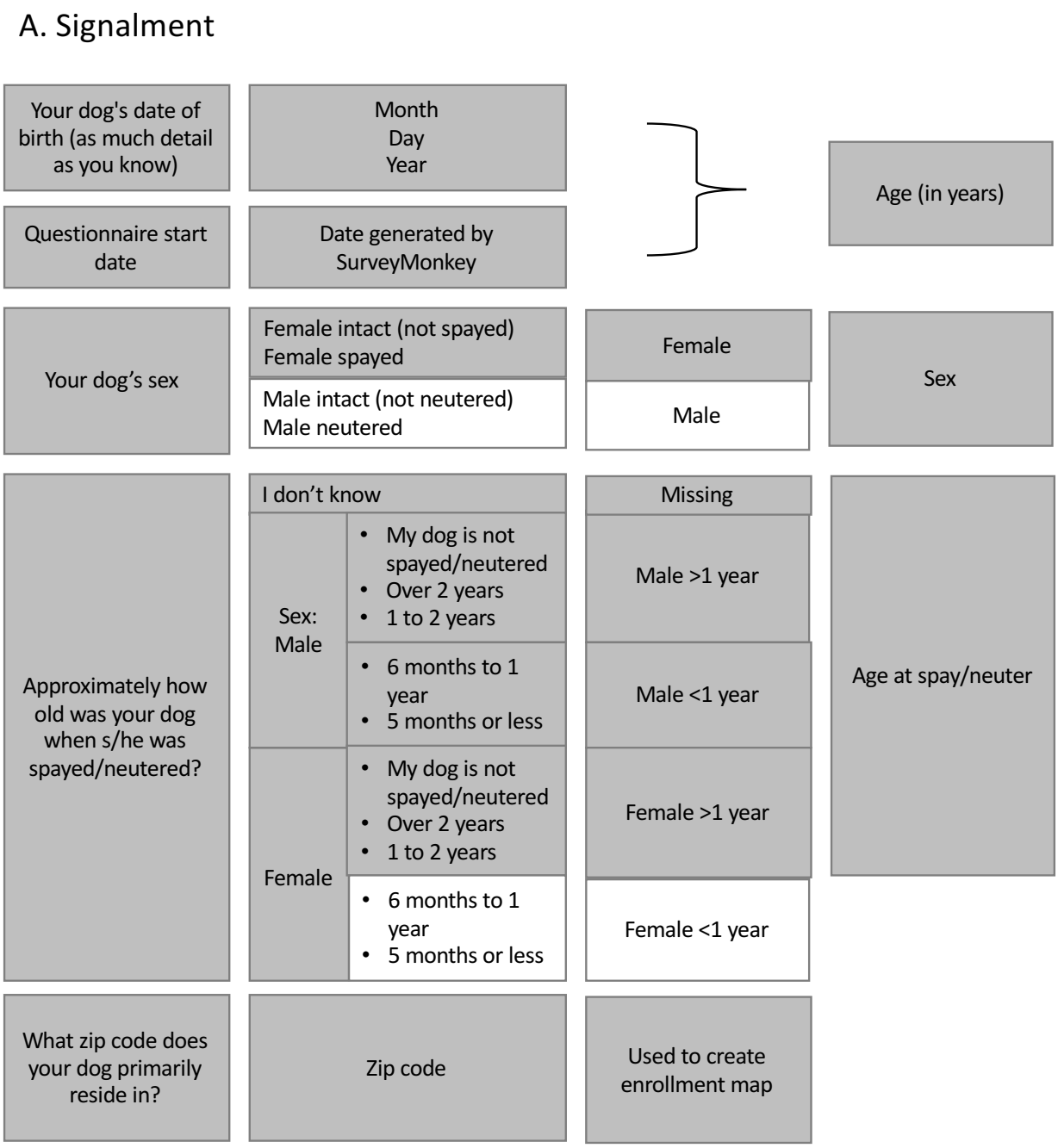
**Suppl. Table 3. Modeling results for TZUS vs. control sensitivity analysis.** *Final model* indicates the model reported as our main results (n=221 TZUS, n=147 controls). *Cancer sensitivity analysis* removed both TZUS and controls with a history of or concurrent non-lymphoma cancer (n=166 TZUS, n=111 controls). % change indicates the percent change in the OR estimate compared to the final model.

| | | Final model | | | | Cancer sensitivity analysis | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | OR | (95% CI) | Indiv p-value | Type3 p-value | OR | (95% CI) | Indiv p-value | Type3 p-value | % change |
| Age at spay/neuter | Female >1yr | 1.07 | (0.59 - 1.95) | 0.831 | 0.050 | 1.42 | (0.71 - 2.87) | 0.325 | | 33% |
| (vs. Female <1yr) | Male <1yr | 0.82 | (0.42 - 1.6) | 0.566 | | 0.91 | (0.40 - 2.05) | 0.815 | | 10% |
| | Male >1yr | 2.22 | (1.13 - 4.37) | 0.021 | | 2.32 | (1.07 - 5.03) | 0.034 | | 4% |
| | Missing | 1.16 | (0.37 - 3.68) | 0.800 | | 1.39 | (0.38 - 5.05) | 0.615 | 0.142 | 20% |
| Bladder infection | Yes (vs. no) | 5.10 | (1.9 - 13.69) | 0.001 | 0.001 | 5.39 | (1.52 - 19.05) | 0.009 | 0.009 | 6% |
| Eye disease | Yes (vs. no) | 1.92 | (0.99 - 3.75) | 0.056 | 0.001 | 2.10 | (0.98 - 4.48) | 0.056 | 0.056 | 9% |




**Suppl. Fig 1. Flow cytometric analysis of peripheral blood samples**. (A) Sample considered diagnostic for TZL due to homogeneous expansion of $CD5^{+}CD45^{-}$ T cells (red cells; TZL). (B) Sample diagnosed as TZUS due to smaller population of $CD5^{+}CD45^{-}$ T cells and absence of lymphocytosis or lymphadenopathy. (C) Sample considered a control; all T cells are CD5+CD45+ (green cells; normal)

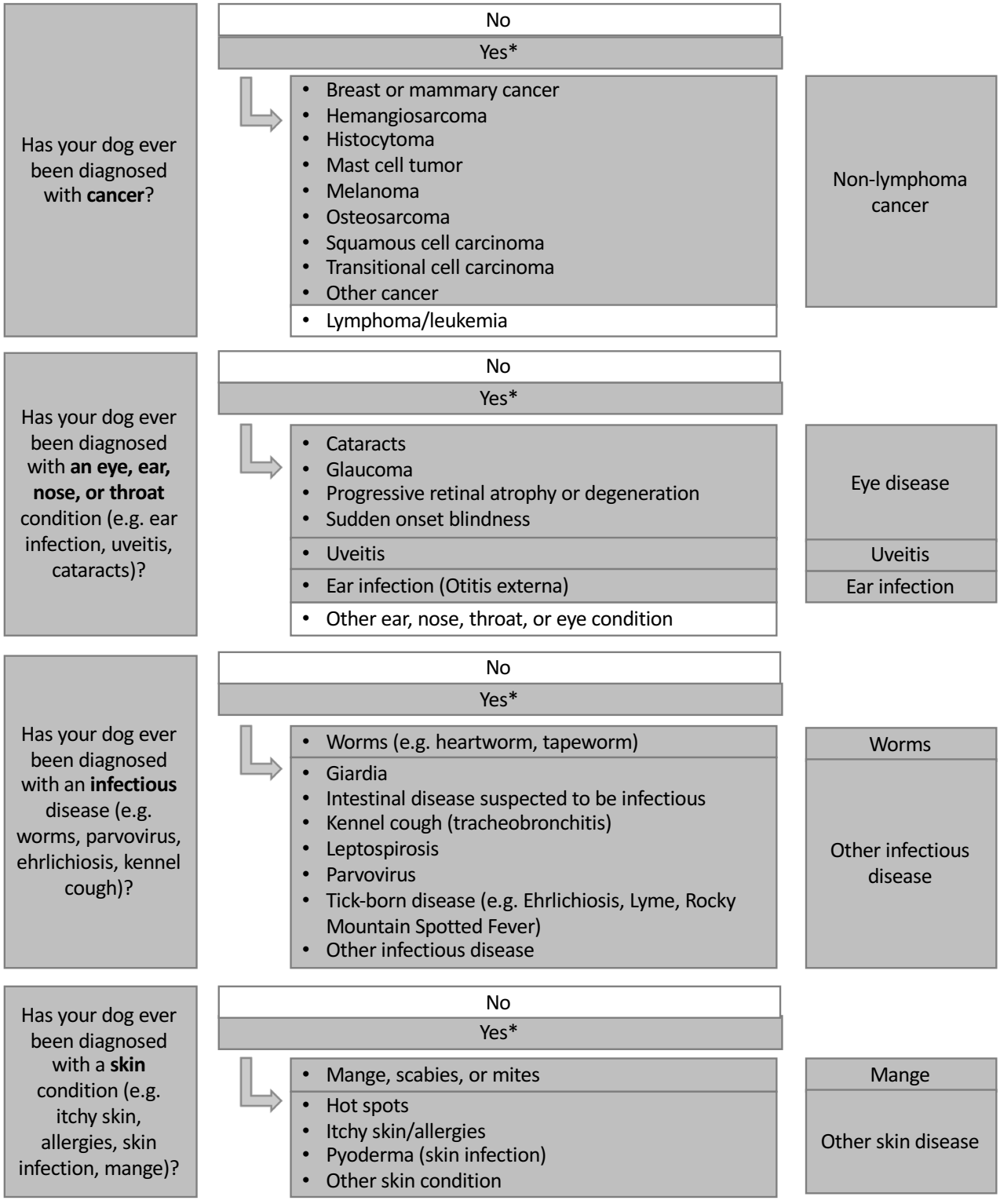
**Suppl. Figure 2. Collapsing of variables from questionnaire for use in analysis.** *Age at diagnosis was captured using the following categories: "<1 year", "1-3 years", "4-6 years", "7-10 years", "Over 10 years", and "Diagnosed with this condition, but can't remember age".

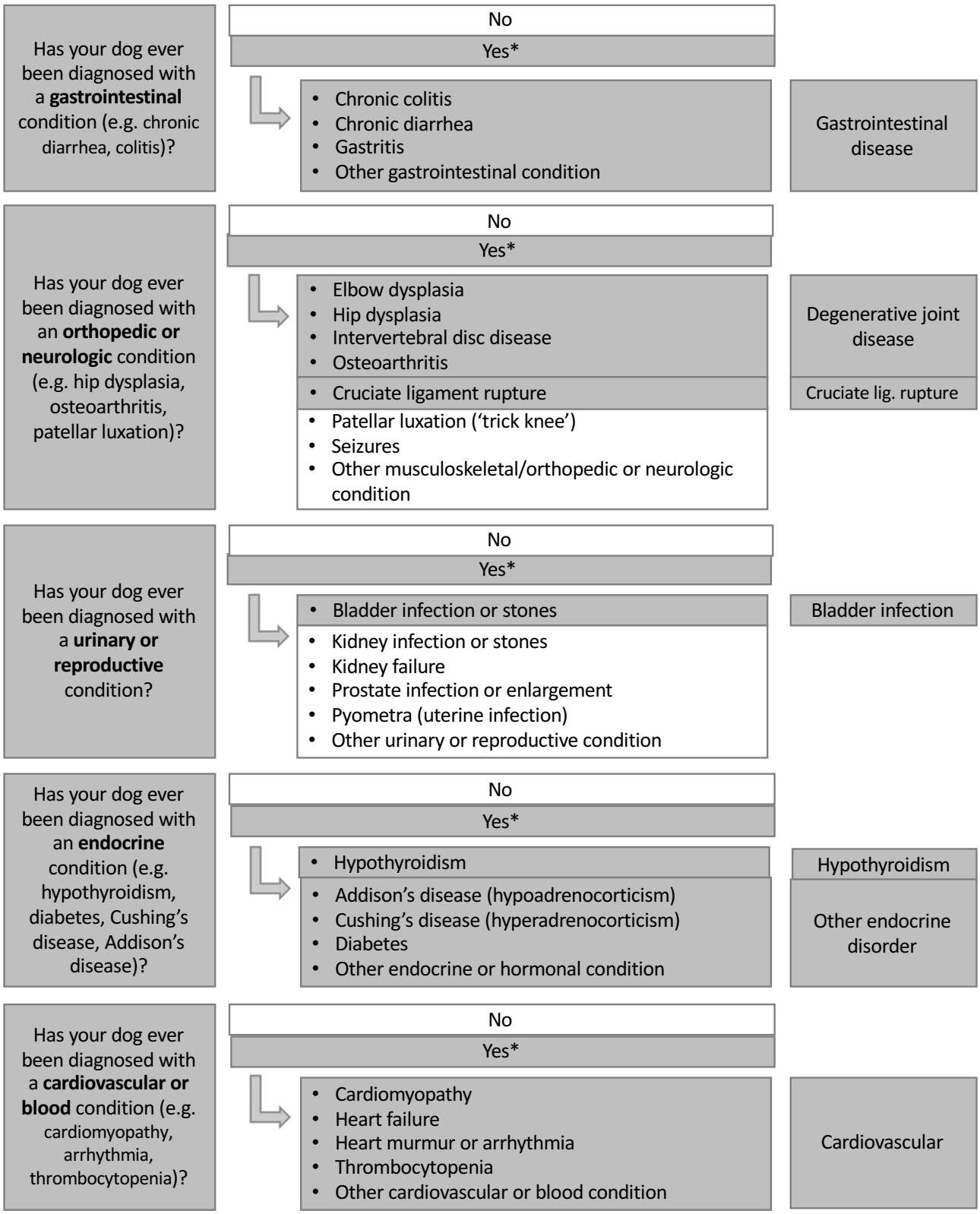


## B. Preventive care

| | | | |
|---|---|---|---|
| How often does your dog use:<br>• Flea preventive treatments<br>• Heartworm preventive treatments | Monthly<br>Seasonally<br>Sporadically | Ever | Flea preventives<br>Heartworm preventives |
| | Never | Never | |
| Have you ever found a tick on your dog? | Yes, once<br>Yes, multiple times | Yes | Tick ever |
| | No | No | |
| Has your dog ever been diagnosed with: | No | | |
| | Yes | | |
| | • Gum disease<br>• Tooth disease (including tooth loss) | | Tooth or gum disease |
| | • Other dental disease | | |
| How many times has your dog had its teeth cleaned by a veterinarian? | 5 or more times<br>3-4 times<br>1-2 times | Ever | Teeth cleaned |
| | Never | Never | |
| How often does your dog receive the following vaccinations?<br>• Rabies<br>• Distemper-Parvovirus combination vaccine<br>• Kennel cough (Bordetella) | Every 6 months<br>Yearly<br>Every 3 years | As directed | • Rabies<br>• Distemper-Parvovirus combination vaccine<br>• Bordetella |
| • Other (incl. Leptospirosis, Lyme, rattlesnake) | Less frequently than every 3 years<br>Never | Not as directed | |
| Has you dog ever had a vaccine reaction (e.g. swelling of the face, paws, or had to return to the veterinarian for treatment after a vaccine)? | Yes | Yes | Vaccine reaction |
| | No | No | |

## C. Health history




Has your dog ever been diagnosed with a **gastrointestinal** condition (e.g. chronic diarrhea, colitis)?
No
Yes*
• Chronic colitis
• Chronic diarrhea
• Gastritis
• Other gastrointestinal condition
Gastrointestinal disease
Has your dog ever been diagnosed with an **orthopedic or neurologic** condition (e.g. hip dysplasia, osteoarthritis, patellar luxation)?
No
Yes*
• Elbow dysplasia
• Hip dysplasia
• Intervertebral disc disease
• Osteoarthritis
Degenerative joint disease
• Cruciate ligament rupture
Cruciate lig. rupture
• Patellar luxation ('trick knee')
• Seizures
• Other musculoskeletal/orthopedic or neurologic condition
Has your dog ever been diagnosed with a **urinary or reproductive** condition?
No
Yes*
• Bladder infection or stones
Bladder infection
• Kidney infection or stones
• Kidney failure
• Prostate infection or enlargement
• Pyometra (uterine infection)
• Other urinary or reproductive condition
Has your dog ever been diagnosed with an **endocrine** condition (e.g. hypothyroidism, diabetes, Cushing's disease, Addison's disease)?
No
Yes*
• Hypothyroidism
Hypothyroidism
• Addison's disease (hypoadrenocorticism)
• Cushing's disease (hyperadrenocorticism)
• Diabetes
• Other endocrine or hormonal condition
Other endocrine disorder
Has your dog ever been diagnosed with a **cardiovascular or blood** condition (e.g. cardiomyopathy, arrhythmia, thrombocytopenia)?
No
Yes*
• Cardiomyopathy
• Heart failure
• Heart murmur or arrhythmia
• Thrombocytopenia
• Other cardiovascular or blood condition
Cardiovascular

## D. Medications, environmental exposures, and diet

| | | | |
|---|---|---|---|
| Other than for treatment of cancer, has your dog ever taken any of the following medications?<br>• Antihistamines (e.g. Diphenhydramine/Benadryl, Chlorpheniramine, hydroxyzine/atarax)<br>• Anti-inflammatories (e.g. Aspirin, Rimadyl, Previcox)<br>• Steroids (e.g. Prednisone, Dexamethasone)<br>• Antibiotics<br>• Oral immunosuppressants (e.g. azathioprine, cyclosporine) | One course<br>Multiple courses<br>Continuous use | Ever | Antihistamines<br>Anti-inflammatories<br>Steroids<br>Antibiotics<br>Oral immunosuppressants |
| | Never | Never | |
| • Non-prescription supplements or alternative therapies<br>• Other medication, including topical | Text box indicating supplement/other medication type | Ever | Omega-3 supplements<br>Other supplements |
| | | Never | |
| On average, how much time does your dog spend on **your lawn** at home? | Over 18 hours per day<br>13-18 hours per day<br>6 -12 hours per day<br>1-5 hours per day | Frequent | Lawn exposure |
| | <1 hour per day<br>Never | Infrequent | |
| On average, how much time does your dog spend in the following areas?<br>• Rural environments?<br>• Parks or other public grassy spaces? | Daily<br>Weekly<br>Monthly | Frequent | Rural environment<br>Parks |
| | Occasionally<br>Never | Infrequent | |
| On average, how often is your dog exposed to:<br>• Lawn chemicals<br>• Cigarette smoke<br>• Paints, solvents, cleaning fluids, etc.? | Daily<br>Weekly<br>Monthly | Frequent | Lawn chemicals<br>Cigarette smoke<br>Other chemicals |
| | Occasionally<br>Never | Infrequent | |
| On average, how often does your dog swim in the following areas?<br>• Ocean<br>• Irrigation ditches, ponds, or canals<br>• Lakes or streams | Daily<br>Weekly<br>Monthly | Frequent | Ocean<br>Irrigation water<br>Lakes/streams |
| | Occasionally<br>Never | Infrequent | |
| What kind of food comprises the majority of your dog's diet? | Commercial dry food (kibble)<br>Commercial canned food<br>Commercial "fresh" or frozen food<br>Home prepared food – cooked<br>Raw diet | | |