Table 1. Multivariable prediction model for 5-month mortality in canines surgically treated for osteosarcoma.

Variables	Odds ratio (95%CI)	Regression coefficients	Standard errors
Intercept		$\hat{\beta}_0$ = -1.2379	0.48
Chemotherapy			
No chemotherapy	Reference	$\hat{\beta}_1$ = 0.0000	
Cisplatin	0.60 (0.31;1.15)	$\hat{\beta}_2$ =-0.5108	0.33
Lobaplatin, carboplatin	0.59 (0.32;1.10)	$\hat{\beta}_3$ =-0.5276	0.31
Doxorubicin	0.52 (0.29;0.95)	$\hat{\beta}_4$ =-0.6539	0.30
Doxorubicin combinations	0.38 (0.21;0.68)	$\hat{\beta}_5$ =-0.9676	0.30
Age (years)	1.03 (0.97;1.09)	$\hat{\beta}_6$ =0.0296	0.03
Weight (kg)	1.02 (1.00;1.03)	$\hat{\beta}_7$ =0.0198	0.01
Male gender	0.79 (0.60;1.05)	$\hat{\beta}_8$ =-0.2357	0.14
Neutered	0.79 (0.54;1.15)	$\hat{\beta}_9$ =-0.2357	0.19
High SALP	1.45 (1.08;1.95)	$\hat{\beta}_{10}$ =0.3716	0.15
Breed			
Other	Reference	$\hat{\beta}_{11}$ = 0.0000	
Rottweiler	0.89 (0.58;1.35)	$\hat{\beta}_{12}$ =-0.1165	0.22
Golden Retriever	0.86 (0.53;1.39)	$\hat{\beta}_{13}$ =-0.1508	0.24
Labrador Retriever	0.81 (0.48;1.37)	$\hat{\beta}_{14}$ =-0.2107	0.27
Greyhound	1.29 (0.70;2.37)	$\hat{\beta}_{15}$ =0.2546	0.31
Doberman	1.47 (0.81;2.69)	$\hat{\beta}_{16}$ =0.3853	0.31
Mixed	0.73 (0.49;1.09)	$\hat{\beta}_{17}$ =-0.3147	0.20
Tumor location			
Other	Reference	$\hat{\beta}_{18}$ =0.0000	
Prox. Humerus	1.54 (1.05;2.25)	$\hat{\beta}_{19}$ =0.4318	0.19
Dist. Femur or Prox. Tibia	0.97 (0.65;1.44)	$\hat{\beta}_{20}$ =-0.0305	0.20
Dist. Radius	0.69 (0.46;1.04)	$\hat{\beta}_{21}$ =-0.3711	0.21

Example patient's predicted logit(5-month mortality risk) = -1.2379 + 0.0000*chemotherapy(0) + 0.0296*7.7 years + 0.0296*44 kg + -0.2357*female(0) + -0.2357* neutered (1) + 0.3716*high salp(1) + -0.0000*Other breed(0) + 0.0000*Other location(0) =-0.0031

Example patient's predicted 5-month mortality risk = $1/(1+e^{(-0.0031)}) = 0.4992$

Numbers represent odds ratios with 95% confidence intervals (95%CI). All odds ratios were adjusted for all other presented variables and a random intercept for a study indicator. This multivariable logistic regression model is based on the cox proportional hazard model described in Schmidt et al., 2013 including the same predictors and using 1295 OS dogs of which 295 died within 5 months collected in 16 studies.

Table 2. Baseline characteristics of 400 canines with osteosarcoma stratified by treatment status.

Variables	No chemotherapy N = 143	Any chemotherapy N = 227	Number of missings N
5-month mortality N (%)	44 (33%)	43 (20%)	36
Chemotherapy			30
No chemotherapy	143 (100%)	0(0%)	
Cisplatin	0(0%)	37(16%)	
Lobaplatin, carboplatin	0(0%)	45(20%)	
Doxorubicin	0(0%)	77(34%)	
Doxorubicin combinations	0(0%)	68(30%)	
Age (years) mean(sd)	8.97(2.98)	8.68(2.72)	26
Weight (kg) mean(sd)	32.20(15.77)	34.40(15.43)	105
Male gender N (%)	75(52%)	127(56%)	21
Neutered N (%)	109(76%)	195(87%)	21
High SALP N (%)	30(58%)	54(47%)	230
Breed			18
Other N (%)	62(43%)	94(41%)	
Rottweiler N (%)	13(9%)	26(11%)	
Golden Retriever N (%)	7(5%)	22(10%)	
Labrador Retriever N (%)	13(9%)	11(5%)	
Greyhound N (%)	5(3%)	16(7%)	
Doberman N (%)	6(4%)	6(3%)	
Mixed N (%)	37(26%)	52(23%)	
Tumor location			38
Other N (%)	73(54%)	82(38%)	
Prox. Humerus N (%)	19(14%)	41(19%)	
Dist. Femur or Prox. Tibia N (%)	24(18%)	48(22%)	
Dist. Radius N (%)	18(13%)	46(21%)	

Data was available on 400 subjects, because 30 had missing information on chemotherapy the columns add up to 370. Serum alkaline phosphatase (SALP); N equals the number of subjects, sd equals the standard deviation. These dogs were originally included in studies by Amsellum, Bacon, Kirpensteijn, Kow and Maritato (co-authors of the current IPDMA).

Table 3. Treatment effect estimates of different chemotherapeutics compared to no chemotherapy on 5-month mortality in dogs surgically treated for osteosarcoma.

	Any chemotherapy	Carboplatin	Cisplatin	Doxorubicin	Doxorubicin combination
Crude model					
Treatment effect	0.43 (0.27; 0.70)	0.30 (0.11; 0.80)	0.66 (0.26; 1.67)	0.34 (0.16; 0.72)	0.43 (0.22; 0.86)
Model adjusted for confounders(except breed)					
Treatment effect	0.45 (0.27; 0.76)	0.27 (0.09; 0.84)	0.59 (0.19; 1.84)	0.34 (0.16; 0.72)	0.42 (0.20; 0.89)
Model additionally adjusting for breed					
Treatment effect	0.48 (0.29; 0.78)	0.32 (0.11; 0.88)	0.72 (0.28; 1.88)	0.38 (0.19; 0.76)	0.45 (0.22; 0.89)
Interaction between chemotherapy and predicted logit(5-month mortality)	0.81 (0.41; 1.62)	0.73 (0.12; 4.53)	1.34 (0.33; 5.37)	0.74 (0.26; 2.09)	0.66 (0.26; 1.72)
adjusted for confounders including breed Treatment effect	3.41 (1.07; 10.84)	4.06 (0.28; 59.07)	3.95 (0.42; 36.91)	6.46 (0.89; 46.66)	2.49 (0.50; 12.43)
Interaction effect					

Results presented as odds ratios (ORs) and 95 % confidence intervals (95%) with no chemotherapy as the reference group, based on 5 studies, including 400 dogs of whom 88 died (for 1 deceased dog chemotherapy treatment was not recorded). All models included a random intercept for study; note that a random intercept was not needed for the carboplatin comparison, which included the single study of Bacon. Besides exploring non-linearity of associations, no model selection was performed and confounders were included based on prior knowledge.

Table 4. Sensitivity analysis including patients surviving the first month. Treatment effect estimates of any chemotherapeutics compared to no chemotherapy on 5-month mortality in dogs surgically treated for osteosarcoma.

	Crude model	Model adjusted for confounders (except breed)	Model additionally adjusting for breed	Interaction between chemotherapy and predicted logit(5-month mortality) adjusted for confounders including breed
Treatment effect	0.68 (0.40; 1.16)	0.74 (0.42; 1.31)	0.81 (0.47; 1.39)	1.13 (0.54; 2.35)
Interaction effect				2.44 (0.66; 8.97)

Results presented as odds ratios (ORs) and 95 % confidence intervals (95%), based on 5 studies, including 340 dogs surviving the first month of follow-up of whom 69 were dead at 5 months follow-up. All models included a random intercept for study membership.