Critical appraisal – Randomised controlled trial questions: Boswood et al, 2016

Introduction	
Are the aims clearly stated?	Yes
Methods	
Is the study design suitable for the aims?	Yes
Which population was studied?	Client owned dogs between 4.1 and 15kg over 6 years of age with MMVD (heart murmur at least 3/6 and on echo evidence of valvular lesion, left atrial to aortic ratio > 1.6, normalised left ventricular internal diameter and diastole > 1.7, and vertebral heart score > 10.5)
Were the treatments randomly allocated? If yes, how was the randomisation done?	Yes Computer software randomization in 1:1 allocation ratio in blocks of 20
Were the groups comparable prior to intervention?	Yes
Was the person who administered the interventions blinded?	Yes
Is it clear what measurements were carried out in the study?	Yes
Were the correct measurements chosen? Do they reflect (or are they strongly related to) the outcome of interest?	Yes

Were previously established validated methods used to make the measurements? (e.g. Glasgow pain score, International Units etc)	Yes
What outcomes were measured?	Primary end point: Time to the development of left sided congestive heart failure (CHF) or euthanasia for a cardiac reason or death presumed to be cardiac in origin Secondary endpoints: Time to the first of one of the events above Time to death of any cause
Are the outcomes clinically relevant?	Yes
Were the outcomes assessed blind?	Yes
Are the statistical methods described?	Yes
Was the statistical significance level stated?	Yes
Was the sample size justified?	Yes
Was ethical approval obtained?	Yes
Are the methods described in enough detail that you could repeat them?	Yes
Results	

Were the basic data adequately described?	Yes
Do the numbers add up? Are all subjects accounted for?	Yes Yes
Was the statistical significance (p value) stated in the results? Is this consistent with the methods? (It should be stated in the sample size or power calculation)	Yes Yes
Were any side effects of the intervention reported if applicable?	Yes
What were the main findings/key results?	162/354 dogs reached the primary end point and the median time for all dogs was 433.5 days (IQR 242-718) The proportion of dogs in each group reaching the primary endpoint was not significant (pimobendan 41.6%, placebo 50%) The estimated median time to primary endpoint was 1228 (95% CI 856-NA) days in the placebo group and 766 (95% CI: 667-875) days in the placebo group. The risk of a dog in the pimobendan group reaching the primary end point was lower than the risk in the placebo group, the hazard ratio was 0.64. Median time to first event in pimobendan group (n=130) was 640 days (95% CI: 555-753) and 406 days (95%, CI:316-527) in the placebo group (n=158) (p< 0.0001) No significant difference in adverse events

Discussion and conclusion	
What do the main findings/key results mean?	The dogs in this study, on average, lived longer if given pimobendan rather than placebo.
Are the negative findings discussed? How are the negative findings interpreted?	Yes
Does the discussion reflect the results?	Yes
Interpretation	
What are the clinical implications of this study? Are the subjects in the study similar to those in the BET/your own?	Pimobendan may increase the survival of dogs with asymptomatic MVD Yes – except the degree of MVD is not as accurate as in the trial
General	
Who funded this study?	Boehringer Ingelheim