Research Protocol

Review title: Nutrition-Based Interventions in Dogs: A Comprehensive Review of Health Outcomes and Implications for Dog Food Recipes

Review Question: In healthy dogs and dogs with common health problems, what are the health-related advantages and disadvantages of nutrition-based interventions?

Searches:

Due to restrictions of Database access, only the PubMed database will be searched. Additionally, hand searching via internet and reference lists of included studies will also be utilised to identify studies for the systematic review.

Refined search using mainly singular terms of interest (e.g. 'probiotics', 'dietary protein' etc.) with OR followed by AND 'dog' and NOT ' human' to filter out studies in humans and ensure the majority of studies that come up are related to dogs in some way.

Searches were restricted to clinical trial and randomised trials only, though relevant reviews will be utilised to aid explanations or to find primary research.

639 results from the following search terms: ((((((((((((((((nutrition) OR (carbohydrate)) OR (fat)) OR (protein)) OR (probiotics)) OR (diet)) OR (food)) OR (macronutrient composition)) OR (macronutrient)) OR (supplement)) OR (nutritional requirement)) OR (dietary)) OR (vitamins)) OR (minerals)) OR (commercial dog food)) OR (dietary fat)) OR (food preparation)) AND (dog)) NOT (human)

Condition or domain being studied*.* Nutrition in dogs on health outcomes. The domain being studied here is companion animal nutritional health, specifically in dogs.

Participants/population:

The inclusion and exclusion criteria for participant population is described below:

Inclusion - Healthy dogs

- Dogs with diseases common among dog breeds.

Exclusion: - Any research not using dogs as study population.

- Dogs with breed specific illnesses

- Dogs with serious, life-threatening illnesses such as cancer, renal failure, severe pancreatitis etc.

Interventions/exposures – Interventions of interest includes nutrition-based interventions incorporated into dogs' food/diet. These can be broadly categorised as interventions related to:

- Probiotics/ prebiotics
- Macronutrients (protein, fat, carbohydrate)
- Protein
- Carbohydrates

- Fat
- Fibre
- Soy/plant-based protein
- Fatty acids
- Amino acids

Studies screened will not be limited to these intervention categories. If a study meets all other inclusion criteria but the intervention does not 'fit' into the pre specified categories, it will still be included, if the study utilises an intervention which manipulates diet in some way.

Comparators/control - Comparator groups eligible for inclusion:

Positive controls – i.e., groups given treatment with known results (usually a product already established on the market), which therefore acts as the control.

Placebo controls i.e., groups that receive the exact same diet as the intervention group in terms of ingredients, dietary composition and analytical constituents BUT their diet will be lacking the key ingredient under investigation

Negative controls i.e., a group in an experiment that does not receive any type of treatment and, therefore, should not show any change during the experiment. E.g., treatment/fed as usual

Historical controls i.e., the practice of using data from past studies or administrative databases to estimate potential response to placebo or standard-of-care treatment among patients in an ongoing study. An example of a historical control is reference ranges.

- A reference range is a set of values that includes upper and lower limits of a lab test based on a group of otherwise healthy subjects. In the case of this re view, reference ranges might be used as a control in studies where the effects of an intervention on haematology or serum chemistry parameters are being investigated. They are then able to compare the values obtained from their study with already established, recommended reference ranges.

Comparisons of different interventions – studies comparing different interventions without a traditional control will also be included.

Types of study to be included:

To assess the beneficial effects of nutritional interventions in dogs, we will be including randomised clinical trials with study designs including parallel groups, crossover, cross-sectional, observational, factorial and Latin square. We will not be including case studies due to the limited generalisability of results form these studies.

Context

Main outcomes

The most important outcomes for this review will be the assessment of the benefits or harms of particular nutritional interventions. These outcomes may fall under the following broad categories:

- Gut health/gut microbiome
- Stool quality
- Osteoarthritis/joint mobility
- Dermatitis
- Diarrhoea

- Palatability/preference
- Safety/tolerability
- Digestibility of foods
- Effect of food preparation and storage techniques

It should be noted that outcomes will not influence the inclusion or exclusion of studies in this review.

Additional outcomes There are no prespecified additional outcomes for this review

Data extraction (selection and coding)

Title and abstract screening and full text screening using Covidence. Each study will be independently screened for eligibility by 2 reviewers using an inclusion and exclusion criteria. Reviewers will be blinded to each other's decisions unless conflicts arise. In the rare instance that conflicts cannot be resolved between reviewers, then an independent third party will evaluate the issue and make a final decision.

Data extraction will be performed on Covidence using a customised data extraction form created following the Cochrane systematic review guidelines. As with the screening stage, 2 reviewers will independently collect data from each study and will be blinded to each other's decisions until consensus. The form will collect data on the following:

- Reviewer and study identifying details (including objectives of the study)
- Study methods (including ethics, trial design, info on blinding)
- Participant characteristics
- Interventions (including details of main interventions and control interventions, trial environment and attrition)
- Outcomes (including how these were measured – the outcomes to be extracted will be pre-specified after full text screening.)
- Baseline data (if available for the specified outcomes).
- Results (including the time point of results, the measure of variability used, the number of participants per outcome, information on p values, confidence intervals and statistical analysis used).

If any of the studies included for data extraction have missing data that is essential to the review, then study authors will be contacted, if we are unable to uncover missing data the study will be excluded from the review.

Once consensus on the data extraction is complete, the extracted data will be saved as an excel spreadsheet ready for data synthesis and analysis.

Risk of bias assessment A formal risk of bias assessment will be performed on all studies. The Cochrane risk of bias tools for either parallel trials or crossover trials will be used for randomised studies. For non-randomised studies the ROBIN-s tool will be used. For cross-sectional studies the AXIS tool will be used.

Strategy for data synthesis

Where possible, outcome data will be expressed as Standardised Mean Difference (SMD) and pooled in a pairwise random effects meta-analysis model, to take into account possible heterogeneity among studies.

Prior to analysis data will be synthesised using a categorisation system which will involve searching for consistency between study interventions and outcomes at a broad level then determining if consistency is shared at more specific levels. For example, studies investigating the effects of 'Bacillus Coagulans' would fall under the broad category 'probiotics', the subcategory would be 'Bacillus Coagulans'. This can be further subcategorised by the dosage level of 'Bacillus Coagulans' used.

This categorisation system will aid in grouping studies for data synthesis, as it will be clear at which level study interventions and outcomes are consistent enough to be pooled together within a single meta-analysis. If study interventions only reach consistency at a broad level e.g., using probiotics as an intervention, these will still be pooled together in a single meta-analysis with the type of probiotic and dosage explored as effect modifiers, to answer the question - 'On average, which probiotic is the most beneficial and at what dosage?'

Data from a minimum of 2 studies will be accepted for synthesis. This low number was chosen due to the possibility of large variation in interventions among studies found for the review.

Analysis of subgroups or subsets

In order to maximize the potential to synthesize data, where necessary data will be synthesised on a broad level, e.g., synthesising data from studies using different measures of the same outcome domain, then performing a subgroup or sensitivity analysis to examine if the effects are modified by, or robust to, the type of measurement method or tool.

Type and method of review.

This is an independent review undertaken in order to aid in the development of a healthy, complete dog food.