Quality of reporting of clinical trials in dogs and cats: An update

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Abstract

Background: Comprehensive reporting of clinical trials is essential to allow the trial reader to evaluate the methodological rigor of the trial and interpret the results. Since publication of the updated Consolidated Standards of Reporting Trials (CONSORT) guidelines for reporting of parallel clinical trials in humans, extensions for reporting of abstracts and crossover trials have been published.

Objectives: To describe the types of trials using dogs and cats published from 2015 to 2020 and to evaluate the quality of reporting of a sample of recently published parallel and crossover trials.

Animals: None.

Methods: A comprehensive search was conducted to identify parallel or crossover design clinical trials using dogs and cats published from January 1, 2015 onwards. Quality of reporting was evaluated on a subset of trials published during 2019. The reporting of items recommended in the CONSORT reporting guidelines for abstracts, parallel trials, and crossover trials was evaluated independently by 2 reviewers using standardized forms created for this study. Disagreements among reviewers were resolved by consensus. Results were tabulated descriptively.

Results: The frequency of reporting of trial features varied from low to high. There remain deficiencies in the quality of reporting of key methodological features and information needed to evaluate and interpret trial results.

Conclusions and Clinical Importance: There is still a need for authors, peer-reviewers, and editors to follow reporting guidelines such as CONSORT to maximize the value of clinical trials and to increase confidence in the validity of the trial results.

KEYWORDS
companion animals, CONSORT statement, trial reporting

INTRODUCTION

Well-conducted randomized controlled trials provide the highest level of evidence for evaluating the efficacy of a treatment, when it is
ethical and feasible to allocate study subjects to treatment groups. The ability of the reader of a trial to evaluate the methodological rigor with which the trial was conducted, as well as to interpret the trial results, is dependent on the trial authors clearly and accurately reporting the methods and the results of the trial. To address issues related to deficiencies in reporting in human health trials, the Consoli-
dated Standards of Reporting Trials (CONSORT) statement, developed by expert consensus, was published in 2001 to provide guidance on reporting of parallel trials. The CONSORT statement comprises 22 items that should be reported in all trial reports. The CONSORT document consists of a publication describing the process of developing the guidelines\(^1\) and a longer explanation and elaboration docu-
ment.\(^2\) A systematic review evaluating the impact of the CONSORT statement was published in 2012.\(^3\) The authors of this review reported that journal endorsement of the CONSORT statement appeared to benefit the completeness of reporting of the trials that they published.

Although developed for human trials, the CONSORT guidelines might be applied to clinical trials in animals. An evaluation of reporting of clinical trials in dogs and cats using the CONSORT statement items identified substantive deficiencies in reporting of important features.\(^4\) More recently, trial methodology and reporting were evaluated in 163 trials in tumor-bearing dogs.\(^5\) The authors of this study also noted concerning deficiencies in reporting, including the observation that over 70% of trials did not identify the primary outcome. Blinding was comprehensively reported in only one-third of 195 randomized trials published between 2004 and 2010.\(^6\) Thus, there is a clear need to improve reporting of clinical trials using dogs and cats. Indeed, the Journal of Veterinary Internal Medicine explicitly states that the CON-
SORT reporting guidelines should be followed.\(^7\)

In the past decade, there have been several new developments related to reporting of clinical trials which are applicable to small animal trials. An updated version of the CONSORT statement was published in 2010,\(^8,9\) and extensions to the CONSORT statement have been published for reporting of abstracts\(^10\) and for reporting of crossover trials.\(^11\) Given these developments in trial reporting, and the evidence of ongoing issues of inadequate reporting, there is a need to re-evaluate the reporting of clinical trials in dogs and cats to identify areas where improvements in reporting are warranted.

Therefore, the objectives of this study were:

1. To describe the types of clinical trials using dogs and cats published from 2015 to 2020.
2. To evaluate the quality of reporting of a sample of recently published parallel and crossover trials in dogs and cats.

2 | METHODS

The following definitions were used throughout this study:

- A clinical trial was defined as a controlled experiment conducted in live animals to prevent or treat a naturally occurring disease or condition, in which the interventions were intended for use in dogs or cats.
- A parallel trial was defined as a clinical trial in which the study units were allocation to 2 or more intervention groups with each study unit allocated to a single intervention group.
- A crossover trial was defined as a clinical trial in which each study unit serves as its own control by being assigned to each of the intervention groups at different time periods.

2.1 | Eligibility

Trials eligible for inclusion to address objective 1 were controlled trials with 2 or more concurrent intervention groups, using a parallel or crossover trial design, conducted in live dogs, cats, or both where dogs or cats were the target species (ie, not evaluated solely as a model for a human intervention or disease condition) and published in English from 2015 and 2020. Before-and-after trials, trials with delib-
erate exposure to the pathogen of interest or deliberate disease induction and trial protocols were not eligible. Trials meeting these eligi-
bility criteria, published in 2019, and not solely evaluating pharma-
cokinetics, bioavailability, or safety were used to address objective 2. Restricting objective 2 to trials published in 2019, and to trials that did not solely evaluate pharmacokinetics, bioavailability, or safety, was based on feasibility of evaluating the anticipated number of trials within available resources. No sample size calculations were con-
ducted as the study was not designed to allow statistical comparisons with the results of previous studies of reporting quality.

2.2 | Search for relevant trials

Searches to identify eligible trials were conducted on May 5, 2020 in MEDLINE (via PubMed) and CAB Direct (via the University of Guelph Library interface). The search was restricted to publications from 2015 to the date of the search. No language or study design filters were applied at the search stage.

The search terms were structured around species (cat or dog), study design (trials), and interventions. The searches were limited to search terms used in the title or abstract to restrict the results to a manageable number of citations. The full search string, as applied in MEDLINE via PubMed, is shown in Table 1.

2.3 | Selection of eligible trials

Four individuals were involved in selection of eligible trials (J. M. Sargeant, M. Plishka, S. C. Totton, E. R. Vriezen). Each article was assessed for eligibility by 2 of these individuals working independently, based on information provided in the title or abstract, with any disagree-
mements resolved by consensus. An eligibility screening form was created in DistillerSR (Evidence Partners Inc., Ottawa, Ontario) and included the fol-
lowing questions:
T A B L E 1  Search string applied to MEDLINE to identify clinical trials in cats or dogs published after 2015

| Population terms: | Number of trials |
|-------------------|------------------|
| (`dogs`)[MeSH Terms] OR `dogs`[All Fields] OR `dog`[All Fields] OR (`cats`)[MeSH Terms] OR `cats`[All Fields] OR `cat`[All Fields] | 1218 |
| `canine`[All Fields] OR `canines`[All Fields] | 899 |
| `felidae`[MeSH Terms] OR `felidae`[All Fields] OR `feline`[All Fields] | 319 |
| Linked to population data restriction using “AND” | 69 |
| `clinical trials as topic`[MeSH Terms] OR (`clinical`[All Fields] AND `trial`s[All Fields] AND `topic`[All Fields]) OR `clinical trials as topic`[All Fields] OR `trial`s[All Fields] OR `trialed`[All Fields] OR `trialing`[All Fields] OR `trials`[All Fields] OR `RCT`[All Fields] OR `random`[All Fields] | 230 |
| Linked to intervention terms using “AND” | 186 |
| (`drug`)[Title/Abstract] OR `surg`[Title/Abstract] OR `vacc`[Title/Abstract] OR `antibiotic`[Title/Abstract] OR `antimicrob`[Title/Abstract] OR `intervention`[Title/Abstract] OR `treatment`[Title/Abstract] | 222 |
| Linked to publication data restriction using “AND” | 237 |
| January 1, 2015:3000/12/31[Date–Publication] | 246 |

Note: For clarity of presentation, population, trial, outcome, and publication date terms are separated in this table.

1. Does the title or abstract describe a study in dogs and or cats (not including animal models of human interventions or illnesses)?
2. Does the title or abstract describe a controlled trial in live animals (at least 2 groups and investigator allocation to group) with natural exposure to the outcome (the disease or condition of interest) was not deliberately induced by the investigator?
3. Is the publication available in English?

If both reviewers agreed that the answer to any 1 of the above questions was “no,” the citation was excluded from further consideration. The first 200 citations were evaluated by all individuals involved in conducting eligibility screening to ensure clarity of questions and for training purposes.

2.4 Data collection

For all references passing eligibility screening, data were collected for descriptive purposes on the year of publication, species, and trial type based on an evaluation of the information provided in the citation information, title, or abstract (Table 2). Data collected were undertaken by the same 4 individuals who performed trial selection. Two reviewers working independently extracted this information from each trial using a structured form created in DistillerSR, with any disagreements resolved by consensus. The form was applied to the first 50 citations by all 4 reviewers to ensure clarity of the questions.

Then, reporting characteristics were evaluated based on the full text for parallel and crossover trials published in 2019 in dogs or cats using separate forms created in DistillerSR. The comprehensiveness and clarity of the questions were evaluated by all authors on 4 manuscripts. After this testing of the data extraction forms, 2 reviewers working independently assessed each trial, with any disagreements resolved by consensus. An initial question confirmed eligibility based on an evaluation of the full text. If more than 1 trial was reported within an article, only 1 eligible trial from within that article was categorized. To select this trial, the following criteria were used: if an article described 1 or more trials focused on safety or pharmacokinetics as well as trials evaluating efficacy, the trial evaluating efficacy was selected; if trials reported within the same article were conducted in both healthy animals and animals with the health condition of interest, the latter trial was used; if more than 1 trial within an article used animals with the health condition of interest, the first trial described in the methods section was used.

For all parallel trials eligible after full-text review, data were extracted on study characteristics including species evaluated in the trial, body system or condition of interest, intervention type, and outcomes evaluated in the trial (Table 3). This information was used to describe the range of clinical trials evaluated for completeness of reporting.

For evaluating reporting characteristics related to the title and abstract for each parallel trial, we created structured questions based on the recommended reporting items from the CONSORT extension for abstracts10 with a few minor wording changes to increase the relevance to trials conducted using dogs and cats (eg, “participant” changed to “study subject”; Table 4). Based on the assumption that few authors would have designated a primary outcome in the title or abstract, we modified the question “Did authors present results for the primary outcome?” to “Did authors present results for 1 or more
| TABLE 3  | Descriptive information on 196 trials in dogs or cats published in 2019 |
|----------|------------------------------------------------------------------------|
|          | Parallel trials (N = 143)                                              | Crossover trials (N = 53) |
| Species  | Dog                                                                     | 109                         | 37 |
|          | Cat                                                                     | 34                          | 16 |
| Type of study subject | Client owned or shelter, with condition of interest | 80                          | 5  |
|          | Client owned or shelter, healthy                                       | 31                          | 6  |
|          | Research animal, with condition of interest                             | 2                           | 1  |
|          | Research animal, healthy                                               | 13                          | 31 |
|          | No information provided                                                 | 17                          | 10 |
| Reported trial descriptors (title, abstract, methods, results)²  | Pilot/preliminary                                                      | 13                          | 4  |
|          | Proof of concept                                                        | 2                           | 1  |
|          | Equivalence                                                             | 0                           | 0  |
|          | Noninferiority                                                          | 6                           | 0  |
|          | Superiority                                                             | 0                           | 0  |
|          | Pragmatic                                                               | 0                           | 0  |
|          | Cluster randomized                                                      | 1                           | 0  |
|          | Efficacy trial                                                          | 4                           | 0  |
|          | None of the above                                                       | 120                         | 48 |
| Body system or condition of interest | Anesthesia/sedation                                                      | 14                          | 12 |
|          | Behavioral/anxiety                                                      | 2                           | 2  |
|          | Cardiovascular                                                          | 19                          | 12 |
|          | Dental                                                                  | 3                           | 0  |
|          | Endocrine                                                               | 8                           | 2  |
|          | Ocular                                                                  | 7                           | 4  |
|          | Fleas/ticks                                                             | 3                           | 0  |
|          | Gastrointestinal                                                        | 18                          | 11 |
|          | Hepatic                                                                 | 0                           | 1  |
|          | Musculoskeletal                                                         | 14                          | 1  |
|          | Nervous system                                                           | 8                           | 2  |
|          | Obesity                                                                 | 2                           | 0  |
|          | Other parasites                                                          | 8                           | 0  |
|          | Pain management                                                          | 18                          | 4  |
|          | Renal                                                                   | 1                           | 0  |
|          | Respiratory                                                             | 0                           | 2  |
|          | Skin/hair/fur                                                           | 9                           | 0  |
|          | Urinary/reproductive                                                    | 9                           | 0  |
| Type of intervention          | Acupuncture                                                             | 2                           | 3  |
|          | Anesthesia/sedation                                                      | 12                          | 13 |
|          | Diet                                                                    | 4                           | 3  |
|          | Flea/tick treatment                                                      | 3                           | 0  |
|          | Management/behavior modification                                         | 1                           | 0  |
|          | Nonpharmaceuticalb                                                       | 35                          | 10 |
|          | Parasite (not flea/tick) treatment                                       | 10                          | 0  |
|          | Pain control                                                            | 8                           | 2  |
|          | Pharmaceuticalc                                                          | 53                          | 22 |
|          | Spay/neuter methods                                                      | 2                           | 0  |
|          | Surgical techniques                                                      | 8                           | 0  |
|          | Vaccine                                                                 | 5                           | 0  |
A question on whether or not the funding source was described in the title or abstract was not included, as this was felt to be a journal decision. Information on whether or not the funding source was reported anywhere in the article was collected. For the reporting characterization of information related to objectives, methods, results, discussion, and aspects of the trial related to funding and transparency, the questions were informed by the CONSORT 2010 statement. Reporting of each item was evaluated using 1 or more questions with fixed-choice responses (Tables 5 and 6). Questions related to CONSORT items 1a or 1b were not included because these items pertain to reporting in the title and abstract; these aspects were addressed using the CONSORT extension for abstracts as described above. Reporting of CONSORT items 2a (scientific background and explanation of rationale), 21 (generalizability of trial findings), or 22 (interpretation), also were not evaluated, as we felt that completeness of reporting of these items, although they are important to address in a trial report, would be subjective and therefore difficult to evaluate.

The same data were collected for crossover trials in dogs or cats published in 2019. The data characterization form included the same questions as the form for parallel trials, with additional questions added for 3 CONSORT items to incorporate modifications for crossover trials as proposed in the CONSORT extension for crossover trials (Tables 5 and 6).

Data were summarized descriptively with cross tabulation using the pivot table function of Excel Version 16.44 (@2020 Microsoft).

### RESULTS

The search identified 6050 unique references, of which 1190 were eligible after title and abstract screening (Figure 1). Year of publication, species, and trial type are summarized for these trials in Table 2, based on information provided in the title and abstract. The number of trials published per year and meeting our eligibility criteria ranged from 186 to 246, and the majority of trials employed a parallel design. Of the 933 parallel trials, 897 compared treatment groups between animals and 36 trials compared treatment groups within animals (eg, comparing treatments between eyes or limbs within the same animal). Assessing bioavailability or pharmacokinetics was the sole purpose of 28 of the parallel trials, and evaluating safety was the sole purpose of 41 of the parallel trials. For the 257 crossover trials, assessing bioavailability or pharmacokinetics was the sole purpose of 56 and evaluating safety was the sole purpose of 6 trials.

There were 143 parallel trials and 53 crossover trials published in 2019 using dogs or cats and not solely evaluating pharmacokinetics.
bioavailability, or safety (Figure 1). Descriptive information for these trials is presented in Table 3. There was a wide range of body systems, intervention types, and outcome types represented by these trials.

Trial descriptors, such as “proof of concept” or “non-inferiority” were rarely used in the titles and abstracts (3/196 and 6/196, respectively). Although the majority of trials (170/196) included an explicit
| TABLE 5  | Reporting of information in the objectives statement and methods section for 196 trials, based on CONSORT reporting guidelines or the CONSORT extension for reporting of crossover trials |
|----------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|          | Parallel trials (N = 143) | Crossover trials (N = 53) |
| **CONSORT item 2b: Specific objective or hypothesis** | | |
| Specific objective or hypothesis provided | Yes | 140 |
| No | | 53 |
| **Methods** | | |
| **CONSORT item 3a: Description of trial design (such as parallel, factorial) including allocation ratio** | | |
| Trial described as parallel or crossover | Yes | 7 |
| No | | 39 |
| Allocation ratio described | Yes | 45 |
| No | | 6 |
| Number of (crossover) time periods reported | Yes | NA—crossover only |
| No | | 52 |
| Duration of time periods reported | Yes | NA—crossover only |
| No | | 53 |
| Duration of washout period reported | Yes | NA—crossover only |
| No | | 49 |
| Justification for washout period length provided | Yes | NA—crossover only |
| No | | 7 |
| **CONSORT item 3b: Important changes to methods after trial commencement (such as eligibility criteria), with reasons** | | |
| Important changes to methods after trial commencement described | Yes, changes to intervention | 12 |
| Yes, changes to sample size | | 4 |
| Yes, changes to recruitment or allocation | | 3 |
| Yes, stated there were no changes | | 0 |
| No information provided | | 126 |
| **CONSORT item 4a: Eligibility criteria for participants** | | |
| Eligibility of study subjects described | Yes | 124 |
| No | | 46 |
| **CONSORT item 4b: Settings and locations where the data were collected** | | |
| Settings described (eg, client home, veterinary practice) | Yes | 100 |
| No | | 17 |
| Number of settings described | Yes | 94 |
| No | | 17 |
| NA—did not describe settings | | 6 |
| **Geographic region described** | Yes | 79 |
| No | | 11 |
| **Dates when trial conducted described (months and years)** | Yes | 44 |
| No | | 2 |
| **CONSORT item 5: The interventions for each group with sufficient details to allow replication, including how and when they were actually administered** | | |
| Each intervention group explicitly described | Yes | 141 |
| No | | 53 |
| Person administering the interventions identified | Yes | 63 |
| No | | 18 |
(Continues)
### TABLE 5 (Continued)

| CONSORT item 6a: Completely defined prespecified primary and secondary outcome measures, including how and when they were assessed | Parallel trials (N = 143) | Crossover trials (N = 53) |
|---|---|---|
| Primary outcome identified, or outcome provided for sample size calculation | Yes | 66 |
| No | 73 |
| NA—only 1 outcome | 4 |
| If repeated measures, primary time point identified | Yes | 28 |
| No | 90 |
| NA, measurements at single time | 25 |
| Described how outcome(s) were measured | Yes | 139 |
| No | 4 |
| Person measuring outcome(s) identified | Yes | 85 |
| No | 58 |
| Timing of outcome measurements(s) described | Yes | 139 |
| No | 4 |

| CONSORT item 6b: Any changes to trial outcomes after the trial commenced, with reasons |
|---|
| Whether or not any changes to outcome measures described | Yes | 2 |
| No | 141 |

| CONSORT item 7a: How sample size was determined |
|---|
| Described how sample size was determined | Yes, provided calculation | 48 |
| Yes, no calculation but provided explanation | 15 |
| No | 80 |
| Accounted for within-animal variability in calculation | Yes | NA—crossover only |
| No | 16 |
| NA – no sample size calculation | 35 |

| CONSORT item 7b: When applicable, explanation of any interim analyses and stopping guidelines |
|---|
| Explanation of interim analysis or stopping guidelines | Yes | 2 |
| No | 141 |

| CONSORT item 8a: Method used to generate the random allocation sequence |
|---|
| Allocation described as random | Yes, called random | 127 |
| Yes, called random systematic | 0 |
| No, stated nonrandom | 12 |
| No information provided | 4 |
| Random sequence generation described | Yes | 80 |
| No | 47 |
| NA—not described as random | 16 |

| CONSORT item 8b: Type of randomization; details of any restriction (such as blocking and block size) |
|---|
| Any restrictions described | Yes | 43 |
| No | 100 |

| CONSORT item 9: Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned |
|---|
| Allocation concealed | Yes, stated or clearly described | 13 |
| No information given | 126 |
| No, stated not concealed | 4 |
| Mechanism to conceal allocation described | Yes | 13 |
| No | 0 |
| NA—did not conceal allocation or no information | 130 |
statement that ethical approval for the use of animals was obtained, whether or not ethical approval was obtained was not reported in 22 parallel and 4 crossover trials. The sample size for this study was not powered to test specific hypotheses and so inferential statistical testing was not performed. However, some qualitative observations on the descriptive information are provided. The majority of parallel trials were in client-owned animals (80/143 parallel trials), whereas crossover trials tended to be conducted using research animals (31/53 crossover trials). Pharmaceuticals were the most common type of intervention for both trial types (53/143 and 22/53 for parallel and crossover trials).
| CONSORT item | Parallel trials (N = 143) | Crossover trials (N = 53) |
|--------------|---------------------------|--------------------------|
| **Results**  |                           |                          |
| CONSORT item 13a: For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analyzed for the primary outcome |                           |                          |
| Intended for participation | 6 | 0 |
| Enrolled 1 or more subjects | 11 | 0 |
| Had subjects included in analysis | 7 | 0 |
| NA, single study site | 81 | 17 |
| Settings not described | 43 | 36 |
| Numbers provided for study subjects in each intervention group |                           |                          |
| Number assessed for eligibility | 34 | 5 |
| Number assigned to groups | 132 | 53 |
| Number receiving intervention | 93 | 35 |
| Number included in the analysis | 112 | 46 |
| None of the above | 0 | 0 |
| CONSORT item 13b: For each group, losses and exclusions after randomization, together with reasons |                           |                          |
| Reason for sites not enrolling study subjects provided |                           |                          |
| Yes | 2 | 0 |
| No | 11 | 0 |
| NA—single site | 81 | 17 |
| NA—reported all sites enrolled | 6 | 0 |
| Settings not described | 43 | 36 |
| Number lost to follow-up after randomization provided by group with reasons |                           |                          |
| Yes | 41 | 15 |
| No | 44 | 8 |
| NA, no losses | 58 | 30 |
| CONSORT item 14a: Dates defining the periods of recruitment and follow-up |                           |                          |
| Length of follow-up for study subjects described |                           |                          |
| Yes | 141 | 51 |
| No | 2 | 2 |
| CONSORT item 14b: Why the trial ended or was stopped |                           |                          |
| Reason for stopping early or providing interim analysis provide |                           |                          |
| Yes | 2 | 0 |
| No | 0 | 0 |
| NA, not stopped early or interim | 141 | 53 |
| CONSORT item 15: A table showing baseline demographic and clinical characteristics for each group |                           |                          |
| Baseline demographic/clinical characteristics provided by intervention group (and time period for crossover trials) |                           |                          |
| Yes | 96 | 0 |
| No | 47 | 53 |
| CONSORT item 16: For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups |                           |                          |
| Whether analysis was by original assigned groups described |                           |                          |
| Yes, stated intention to treat analysis | 4 | 0 |
| Yes, stated per protocol analysis | 2 | 0 |
| No, but stated all subjects complied with protocol | 2 | 0 |
| No, but unlikely to have protocol deviations | 66 | 32 |
| No, but potential for protocol deviations | 62 | 21 |
| Both ITT and PP analysis conducted | 7 | 0 |
| CONSORT item 17a: For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval) | Parallel trials (N = 143) | Crossover trials (N = 53) |
|---|---|---|
| Results provided only in graphical form | Yes | 0 | 0 |
| No | 143 | 53 |
| Effects by group provided | Yes, effects by group with no measure of precision | 6 | 1 |
| Yes, effects with only P value or P value cut point | 19 | 0 |
| Yes, effects with confidence intervals (±P values) | 5 | 2 |
| Yes, effects with measure of precision (±P values or CI) | 107 | 50 |
| No | 5 | 0 |
| NA, no statistical analysis | 1 | 0 |
| Effect sizes (eg, RR, OR, HR, mean difference) reported | Yes, with only P value or P value cut point | 3 | 0 |
| Yes, with confidence intervals (±P values) | 16 | 2 |
| Yes, effects with measure of precision (±P values or CI) | 2 | 0 |
| No | 121 | 51 |
| NA, no statistical analysis | 1 | 0 |
| If effect sizes given, based on within-participant comparison | Yes | NA – crossover only | 0 |
| No | 0 |
| Unclear | 2 |
| Included variables other than intervention and those associated with nonindependence in analysis | Yes | 20 (reasons provided for 4) | 5 (reasons provided for 2) |
| No | 122 | 48 |
| NA, no statistical analysis | 1 | 0 |
| CONSORT item 17b: For binary outcomes, presentation of both absolute and relative effect sizes is recommended | Absolute and relative effect sizes presented | Yes | 7 | 0 |
| No | 82 | 23 |
| NA, no statistical analysis | 1 | 0 |
| NA, no binary outcome | 53 | 30 |
| CONSORT item 18: Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing prespecified from exploratory | Subgroup analysis described as exploratory | Yes | 3 | 0 |
| No, but stated as planned a priori | 5 | 0 |
| No | 9 | 0 |
| NA, no subgroup analysis | 126 | 53 |
| Results reported for analysis not described in methods | Yes | 11 | 1 |
| No | 132 | 52 |
| If yes, described as exploratory | Yes | 0 | 0 |
| No | 11 | 1 |
| CONSORT item 19: All important harms or unintended effects in each group | Presence or absence of harms or adverse effects reported | Yes | 97 | 37 |
| No | 46 | 16 |
| Discussion | (Continues) |
crossover trials, respectively), with nonpharmaceuticals (35/143 and 10/53) and anesthesia or sedation interventions (12/143 and 13/53) also commonly evaluated.

Tables 4 to 6 provide the results for the reporting of both parallel and crossover trials for information provided in the title or abstract, objectives and methods, and results and discussion, respectively. The proportion of trials reporting the recommended information varied widely between CONSORT items. Some areas, such as reporting the study objectives and hypotheses, the eligibility criteria for study subjects, descriptions of the intervention groups, the method of measuring the outcome(s), the length of follow-up of study subjects, and the statistical methods used to compare groups, generally were well reported. However, other items, including the geographic region, the primary outcome, the justification for the sample size, whether or not allocation was concealed, the numbers needed to follow the flow of study subjects over the course of the trial, baseline demographics by intervention group, and whether or not there was an a priori protocol were not reported in many trials.

4 | DISCUSSION

Clinical trials are a common study design in dog and cat research and our study identified over 200 parallel or crossover trials published annually since 2016. The actual number of trials in dogs and cats published annually is much larger, given our inclusion of English language
trials only and our exclusion of trials in dogs and cats used as animal models of disease, challenge trials, and trials focusing solely on evaluating pharmacokinetics, bioavailability, or safety. Although the majority of the trials employed a parallel design, approximately 20% (257/1190) employed a crossover design. However, despite the importance of clear and transparent reporting of clinical trials, there are still areas where improvement is needed for both parallel and crossover trials conducted in dogs and cats. Given that clinical trials in dogs and cats involve the allocation of animals to treatments that might be inferior, there is a moral imperative to ensure that the results of the trial are usable. Comprehensive reporting is an essential first step in the ability to use the information provided by trial reports.

Our results suggest that, while some trial features are well reported, there still is a need to improve the completeness of reporting. Reporting of key features in the title or abstract is critical for the identification of relevant trials for the reader. Using important trial labels such as “randomized,” “parallel,” or “crossover” in the title and abstract allow for efficient identification of these trial reports by individuals seeking information on interventions or for those conducting systematic reviews. Our finding of reporting deficiencies in the titles and abstract is consistent with a previous evaluation in the veterinary literature. The CONSORT extension for reporting in journal and conference abstracts provides guidance on what information should be included in an abstract. The organization of abstracts and, in some instances, the topics to be included in an abstract might be specified by journal editors. Nonetheless, the CONSORT extension for abstracts provides useful guidance for items that should be reported when possible. Examples of how to address all items in an abstract with short word limits are available and, although the examples are from human trials, might be helpful for authors of veterinary trials.

Comprehensive reporting of the methods and results of clinical trials is important for several reasons; inadequate reporting makes it difficult to determine methodological rigor, interpret trial results, and use trial results for secondary purposes, such as systematic reviews and meta-analyses. Methodological rigor refers to the appropriate design or conduct of trials to reduce the potential for biased results. Items in the CONSORT statement related to the ability of a reader to assess the risk of bias include reporting the method of allocating study subjects to intervention groups, whether allocation was concealed, the use of blinding, losses to follow-up, and whether analysis was based on intention to treat or per protocol. The frequency of reporting of these items ranged from low (20/216 described whether or not allocation was concealed) to reasonably high (158 reported random allocation to treatment group and 13 reported non-random allocation methods, with only 5 providing no information on the method of treatment allocation). Methodological rigor also includes aspects such as clear identification of a primary outcome, which should be the basis used to adequately power a trial to find meaningful differences.
Our finding that approximately half of the trials evaluated (90 of 191 trials with more than 1 outcome) reported the primary outcome is higher than the 28% of cancer trials in dogs where a primary outcome was identified.5

The ability of the reader to interpret the results of a trial and to assess external validity (generalizability) is captured by items such as descriptions of study subject eligibility, study settings, and geographic regions, as well as explicit descriptions of all intervention groups and methods of measuring the outcomes. Although some of these features were generally well reported, it is concerning that this information still is not universally reported.

The current study did not evaluate possible reasons why researchers did not report the information that is recommended in the CONSORT guidelines. However, reasons might include lack of awareness of the guidelines or a perception that the guidelines are less relevant to trials conducted in dogs and cats. A resource for increasing awareness of, and access to, reporting guidelines for a wide variety of study designs is the Equator Network website,15 which includes a searchable library of reporting guidelines. Similarly, the Meridian Network website16 contains links to the smaller number of guidelines specific to animals; to date this comprises the ARRIVE statement for in vivo animal experiments,17 the REFLECT statement for clinical trials in livestock,18 and the STROBE-Vet statement for observational studies in animal populations.19 Journal editors, in addition to authors and peer-reviewers, have an important role to play in driving change, including the awareness and adoption of reporting guidelines.20 Thus, the promotion of CONSORT guidelines on the JVIM instructions to authors is laudable.

The CONSORT statement was developed for human healthcare trials, and thus is it possible that researchers perceive the guidelines as not entirely applicable to trials conducted in dogs and cats. In veterinary medicine, the REFLECT statement provides reporting guidelines specifically for reporting of clinical trials in livestock species.18 The reporting guidelines, developed by expert consensus, were based on the CONSORT statement but included modified wording and items to address issues specific to trials conducted in livestock populations. The accompanying explanation and elaboration document provides livestock-specific examples and explanations.21 Subsequent evaluations have shown that reporting in livestock trials has improved since publication of the REFLECT statement.22,23 It might be warranted to consider reporting guidelines specifically tailored to clinical trials in dogs and cats.

The results of this study do not necessarily mean that trials were poorly reported; it is possible to have a well-conducted trial that is poorly reported and a poorly conducted trial that is well reported. Devereaux et al.24 contacted authors of published human trials and found that some investigators had used appropriate methodological approaches but did not report the information in their published trial report. In addition, the present study had potential limitations that should be considered when interpreting these results. The individuals evaluating the trials were not blinded to authors names and affiliations. However, each trial was evaluated by 2 reviewers working independently, decreasing the risk of misclassification of reporting criteria. We also only considered trials published in English. It is possible that trials reported in other languages differ in the completeness of their reporting.

5 | CONCLUSIONS

Although the CONSORT reporting guidelines for human health trials have been available for decades, there remain substantial deficiencies in reporting of clinical trials in dogs and cats. Trialists, peer-reviewers, and journal editors all have a role in improving trial reporting to maximize the value of these clinical trials.

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CONFLICT OF INTEREST DECLARATION

J. M Sargeant is a co-author of The REFLECT Statement: Methods and Processes of Creating Reporting Guidelines for Randomized Controlled Trials for Livestock and Food Safety and The REFLECT Statement: Reporting guidelines for randomized controlled trials in livestock and food safety: Explanation and elaboration. No other authors have conflicts of interest to declare.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

Authors declare no IACUC or other approval was needed.

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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SARGEANT ET AL.