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Study protocol: Reporting characteristics of intervention trials of animals published in the Journal of Dairy Science in 2017

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Abstract

Objectives The scope of this cross-sectional observational study is to evaluate prevalence of reporting the 19 objective items of the REFLECT statement checklist (Sargeant et al., 2010), with the primary outcome being prevalence of sample size calculation, in clinical trials published in the Journal of Dairy Science from January to December of 2017. We will also determine risk of bias in individual studies using the Cochrane Risk of Bias 2.0 tools for individually randomized, parallel group trials; cluster randomized, parallel group trials; and individually randomized, cross-over trials (Higgins et al., 2016).

Disciplines

Research Methods in Life Sciences | Veterinary Medicine | Veterinary Preventive Medicine, Epidemiology, and Public Health

Authors

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Expected contributions
KC – screened studies, extracted data
SL – developed proposal, reviewed manuscript
AOC – developed proposal, reviewed manuscript
DR – developed proposal, extracted data, analysed data, prepared manuscript
JS – developed proposal, extracted data, reviewed manuscript
CW – developed proposal, screened studies, extracted data, analysed data, prepared manuscript

Objectives
The scope of this cross-sectional observational study is to evaluate prevalence of reporting the 19 objective items of the REFLECT statement checklist (Sargeant et al., 2010), with the primary outcome being prevalence of sample size calculation, in clinical trials published in the *Journal of Dairy Science* from January to December of 2017. We will also determine risk of bias in individual studies using the Cochrane Risk of Bias 2.0 tools for individually randomized, parallel group trials; cluster randomized, parallel group trials; and individually randomized, cross-over trials (Higgins et al., 2016).

Sample size
Previous work examining reporting characteristics of studies evaluating the comparative efficacy of FDA-registered antimicrobials against naturally acquired BRD (bovine respiratory disease) in weaned beef calves in Canada or the USA found that 36 % of studies published after 2010 reported a sample size calculation (Totten et al., 2018). With an estimated a prevalence of 40 %, 95 % confidence and a 6 % margin of error, we determined a sample size for our study of 219. We conservatively estimated our search terms would require exclusion of 2/3 of papers found, and therefore based our inclusion on a one-year period (2017), whose pilot search resulted in 704 publications, which should yield approximately 230 inclusions.

Study selection and screening

The literature search will be conducted in MEDLINE via OVID (University of Guelph license) with the following string: (AB=(experiment OR study OR studies OR trial OR challenge) AND JN=(Journal of Dairy Science) AND limit to YR="2017"). Search results will be exported into DistillerSR (Ottawa, Ontario, Canada). All title/abstracts will be independently screened by KC and CW for relevance using the following criteria:

1.) Does the title/abstract describe a primary study involving animals or groups of animals as the experimental unit? (N, reject; Y, proceed; Unclear, acquire full text and give Y/N)

2.) Does the title/abstract describe an intervention study with at least one comparator group? (N, reject; Y, include; Unclear, acquire full text and give Y/N)

Studies will be included/excluded using agreement at the form level. Conflicts will be resolved by consensus with mediation by JS if needed.

Data extraction

Data will be extracted in DistillerSR (Ottawa, Ontario, Canada) independently in duplicate. Descriptive information extracted will include: location of the study (country), last author affiliation (department (if applicable) and institution), last author affiliation (country), animal specie(s), location setting (commercial, university/research, not reported), type of study (field trial or challenge study), and study design (parallel group or cross-over). Field trials are defined as those completed in a clinical or field setting (including research herds) which involve investigator control of study unit selection and intervention allocation, but not exposure to disease, whereas challenge studies involve purposive disease exposure. Data from multiple studies presented in a single paper will be extracted separately but in a single form.

Reporting characteristics. Reporting characteristics will be assessed using a comprehensive reporting assessment tool, based on the first 19 items of the REFLECT Statement, developed by Totten et al. (2018) and outlined in Table 1. Some questions were slightly modified to remove specific outcomes of interest based on the objectives of their work. An additional question pertaining to cross-over studies was added. Reporting characteristics will be extracted by two of KC, DR, JS, or CW. Conflicts at the question level will be resolved by consensus with mediation by JS or SL if needed.

Risk of bias. Risk of bias will be assessed independently in duplicate by DR and CW using the Cochrane risk of bias 2.0 tools for individually randomized, parallel group trials, cluster randomized, parallel group trials, and individually randomized, cross-over trials (Higgins et al., 2016). Questions pertaining to blinding of 'participants' (animals/animal groups) were removed as was question 1b (for cluster randomized parallel group trials). All other questions were included as outlined in Table 2. Risk of bias will be assessed by two of KC, DR, JS, or CW with conflicts resolved by consensus with mediation by JS or SL if needed.

Presentation of results

A summary of descriptive information will be used to qualitatively present the breadth of work captured by the study selection and screening. Prevalence of reporting characteristics will be presented in a table summarizing each question. Risk of bias will be presented as prevalence of category of risk of bias judgement for each bias domain.

References

Higgins J.P.T., J.A.C. Sterne, J. Savović, M.J. Page, A. Hróbjartsson, I. Boutron, B. Reeves, S. Eldridge. A revised tool for assessing risk of bias in randomized trials. Cochrane Methods. *Cochrane Database of Systematic Reviews* 2016: 10 (Suppl 1). dx.doi.org/10.1002/14651858.CD201601.
https://sites.google.com/site/riskofbiastool//welcome/rob-2-0-tool

Sargeant, J.M., A.M. O'Connor, I.A. Gardner, J.S. Dickson, M.E. Torrence, I.R. Dohoo, S.L. Lefebvre, P.S. Morley, A. Ramirez, K. Snedeker. 2010. The REFLECT statement: Reporting guidelines for randomized controlled trials in livestock and food safety: Explanation and elaboration. Zoo. Public Health. 57: 105–136

Totten, S.C. J.N. Cullen, J.M. Sargeant, A.M. O'Connor. 2018. The reporting characteristics of bovine respiratory disease clinical intervention trials published prior to and following publication of the REFLECT statement. Prev. Vet. Med. 150:117-125.

Table 1. Data extraction items for reporting characteristics in primary intervention studies published in the *Journal of Dairy Science* in 2017. Questions were developed by Totten et al. (2018), although modifications were made to remove specifically referenced outcomes used in their study. One additional question pertaining to washout periods in cross-over studies was added (italics).

REFLECT Statement checklist item	
1	In the Title and/or Abstract, did the investigators report that the study units were randomly allocated to the interventions?
2	In the Introduction, did the investigators provide a scientific background of the topic and a rationale (explanation) for the study?
3.1	In the Methods, did the investigators report eligibility criteria for the farm/owner/manager?
3.2	In the Methods, did the investigators report study unit (animal or animal group) eligibility?
3.3	In the Methods, was the setting where the data were collected described?
4	In the Methods, did the investigators give precise details of the interventions intended for each group, the level at which the intervention was allocated, and how and when interventions were actually administered?
5.1	Did the investigators report the specific objectives of the study?
5.2	Did the investigators report the specific hypotheses of the study?
6	Did the investigators give clearly defined primary and secondary outcome measures and the levels at which they were measured, and, when applicable, any methods used to enhance the quality of the measurements?
7	Did the investigators report how the sample size was determined and, when applicable, give an explanation of any interim analyses and stopping rules?
N/A	*Was there a washout period(s), and was there a rationale behind the period(s) explained?*
8	Did the investigators report the method used to generate the random allocation sequence at the relevant level of the organizational structure, including details of any restrictions?
9	Did the investigators report the method used to implement the random allocation sequence at the relevant level of the organizational structure, (e.g. numbered containers), clarifying whether the sequence was concealed until interventions were assigned?
10.1	Did the investigators report who generated the allocation sequence?
10.2	Did the investigators report who enrolled study units?
10.3	Did the investigators report who assigned study units to their groups at the relevant level of the organizational structure?
11.1	Did the investigators report whether or not those administering the interventions were blinded?
11.2	Did the investigators report whether or not caregivers were blinded?
11.3	Did the investigators report whether or not those assessing the outcomes were blinded?
11.4	Did the investigators report whether or not those analyzing the data were blinded?
11.5	Did the investigators report blinding (or the absence of blinding) at all?
12	Were statistical methods used to compare groups for all outcome(s), and did the investigators clearly state the level of statistical analysis and methods used to account for the organizational structure (where applicable)?

13	In the Results, did the investigators report the flow of study units through each stage for each level of the organization structure of the study?
14	Did the investigators report dates defining the periods of recruitment and follow-up?
15	Did the investigators report the baseline demographic and clinical characteristics of each group, explicitly providing information for each relevant level of the organizational structure?
16	Did the investigators report the number of study units (denominator) in each group included in each analysis and the results in absolute numbers when feasible?
17	Did the investigators report a summary of results for each intervention group, accounting for each relevant level of the organizational structure, and the estimated effect size and its precision (e.g., 95% confidence interval)?
18	Did the investigators address multiplicity by reporting any other analyses performed, including subgroup analyses and adjusted analyses, indicating those pre-specified and those exploratory?
19	Did the investigators report all important adverse events or side effects in each intervention group?

Table 2. Items from the Cochrane Risk of Bias 2.0 tool (Higgins et al., 2016) used to assess bias in included studies from the *Journal of Dairy Science* in 2017.

	Individually randomized, parallel group trials	Cluster randomized, parallel group trials	Individually randomized, cross-over trials
Bias arising from the randomization process	1.1, 1.2, 1.3	1a.1, 1a.2, 1a.3	1.1, 1.2, 1.3, 1.4, 1.5
Bias due to deviations from intended interventions	2.2, 2.3, 2.4, 2.5, 2.6	2.2, 2.3, 2.4, 2.5a, 2.5b, 2.6	2.2, 2.3, 2.4, 2.5, 2.6, 2.7
Bias due to missing outcome data	3.1, 3.2, 3.3	3.1a, 3.1b, 3.2, 3.3	3.1, 3.2, 3.3
Bias in measurement of the outcome	4.1, 4.2	4.1a, 4.1b, 4.2	4.1, 4.2
Bias in selectin of the reported result	5.1, 5.2	5.1, 5.2	5.1, 5.2, 5.3