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The reporting characteristics of bovine respiratory disease clinical intervention trials published prior to and following publication of the REFLECT statement

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ABSTRACT

The goal of the REFLECT Statement (Reporting guidElines For randomized controLled trials in livEstoCk and food safeTy) (published in 2010) was to provide the veterinary research community with reporting guidelines tailored for randomized controlled trials for livestock and food safety. Our objective was to determine the prevalence of REFLECT Statement reporting of items 1–19 in controlled trials published in journals between 1970 and 2017 examining the comparative efficacy of FDA-registered antimicrobials against naturally acquired BRD (bovine respiratory disease) in weaned beef calves in Canada or the USA, and to compare the prevalence of reporting before and after 2010, when REFLECT was published. We divided REFLECT Statement, items 3, 5, 10, and 11 into subitems, because each dealt with multiple elements requiring separate assessment. As a result, 28 different items or subitems were evaluated independently. We searched MEDLINE® and CABI (CAB Abstracts® and Global Health®) (Web of Science™) in April 2017 and screened 2327 references. Two reviewers independently assessed the reporting of each item and subitem. Ninety-five references were eligible for the study. The reporting of the REFLECT items showed a point estimate for the prevalence ratio > 1 (i.e. a higher proportion of studies published post-2010 reported this item compared to studies published pre-2010), apart from items 10.3, i.e., item 10, subitem 3 (who assigned study units to the interventions), 13 (the flow of study units through the study), 16 (number of study units in analysis), 18 (multiplicity), and 19 (adverse effects). Fifty-three (79%) of 67 studies published before 2010 and all 28 (100%) papers published after 2010 reported using a random allocation method in either the title, abstract, or methods (Prevalence ratio = 1.25; 95% CI (1.09,1.43)). However, 8 studies published prior to 2010 and 7 studies published post-2010 reported the term "systematic randomization" or variations of this term (which is not true randomization) to describe the allocation procedure. Fifty-five percent (37/67) of studies published pre-2010 reported blinding status (blinded/not blinded) of outcome assessors, compared to 24/28 (86%) of studies published post-2010 (Prevalence ratio = 1.5, 95% CI (1.19, 2.02)). The reporting of recommended items in journal articles in this body of work is generally improving; however, there is also evidence of confusion about what constitutes a random allocation procedure, and this suggests an educational need. As this study is observational, this precludes concluding that the publication of the REFLECT Statement was the cause of this trend.

1. Introduction

1.1. Rationale

In science, including veterinary science, there has been a movement toward improving the reporting of research protocols, conduct, and results (Altman et al., 2008; Begley, 2013; Groves and Godlee, 2012; Keiding, 2010; Simera et al., 2010; Simera and Altman, 2009; Sweet, 2014). The rationale for these efforts is to enable the maximum value to be extracted from research results. Randomized controlled trials (RCTs) that are clearly reported allow the clinician to properly assess the efficacy of tested interventions and incorporate that information into

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Table 1
Results of a database search conducted in MEDLINE® (Web of Science™) on 15 April 2017 for a survey of clinical trials conducted in Canada and/or the USA examining the comparative efficacy of at least one FDA-registered antimicrobial against naturally acquired BRD in weaned beef calves. Search dates were restricted to 1970 to present (2017). There were no language or document-type restrictions.

Search no	Search string	# Hits
1	TS = (beef OR bovine OR calf OR calves OR cattle OR cow OR cows OR dairy OR Hereford OR Holstein OR ruminant OR ruminants OR steer OR steers)	443,367
2	TS = (bovine respiratory disease OR Bovine viral diarrhea OR Bovine viral diarrhea virus OR undifferentiated fever OR BRD OR BVD OR BVDV OR *Haemophilus somnus* OR *Histophilus somni* OR IBR OR Infectious bovine rhinotracheitis OR *Mannheimia hemolytica* OR *Pasteurella multocida* OR Pasteurellosis OR respiratory disease OR undifferentiated bovine respiratory disease)	198,197
3	TS = (amoxicillin OR ampicillin OR antibiotic OR antibiotics OR antimicrobial OR antimicrobials OR erythromycin OR ceftiofur OR cloxacillin OR danofloxacin OR enrofloxacin OR florfenicol OR gentamycin OR lincomycin OR oxytetracycline OR penicillin OR spectinomycin OR sulfamethoxazole OR tilmicosin OR trimethoprim OR tulathromycin OR tylosin OR gamithromycin OR danofloxacin OR tildipirosin)	443,841
4	#1 AND #2 AND #3	676

making the best therapeutic and preventive decisions for patients. To improve the reporting of RCTs in human health, the CONSORT Statement (Consolidated Standards of Reporting Trials) was originally developed in 1996 and has been subsequently revised, with the latest version being published in 2010 (Moher et al., 2010; Schulz et al., 2010). The goal of reporting guidelines is to provide authors, reviewers, and editors with a list of items that should be included in a publication to encourage comprehensive reporting.

In 2010, the REFLECT Statement (Reporting guidElines For randomized controLled trials in livEstoCk and food safeTy) was also published. The goal of the REFLECT Statement was to provide the veterinary research community with a reporting guideline tailored for randomized controlled trials conducted in the fields of livestock and food safety (O'Connor et al., 2010b; Sargeant et al., 2010b). The rationale for a livestock-specific reporting guideline was that, although it is feasible to use the CONSORT Statement for RCTs in animals, authors, reviewers and editors might find the reporting guideline easier to adopt if the examples and terminology used were more consistent with livestock production; additionally, there are some features of livestock trials (such as complex organizational levels (e.g., pens, feedlots), different categories of participants (i.e., owners/managers and animals), etc.) that CONSORT does not address. In 2010, the REFLECT Statement was published in 5 journals, and several presentations were made to publicize the goal of the work (O'Connor et al., 2010a, 2010b, 2010c, 2010d, 2010e; Sargeant et al., 2010a, 2010b). Further, a website devoted to the REFLECT Statement was developed and maintained (www.reflect-statement.org). One of the motivators for the REFLECT Statement was empirical evidence of poor reporting in livestock trials (Brace et al., 2010; O'Connor et al., 2010f; Sargeant et al., 2009; Wellman and O'Connor, 2007). Given the goal of reporting guidelines to improve comprehensive reporting, it is of interest to assess if such approaches have made an impact.

1.2. Objectives

Therefore, one objective of this study was to determine the prevalence of reporting of REFLECT items 1–19, with respect to clinical trials conducted in Canada and/or the USA examining the comparative efficacy of FDA-registered antimicrobials against naturally acquired BRD (bovine respiratory disease) in weaned beef calves, published in journals between 1970 and 2017. The rationale for assessing this area was that a large number of RCTs were conducted, and we had previously evaluated the reporting of these studies and discussed the need for improvement (O'Connor et al., 2010f). Although we evaluated the first 19 items of the REFLECT Statement for the current study, items 3, 5, 10, and 11 had to be split into subitems, because each of these dealt with multiple elements that needed to be assessed separately. As a result, a total of 28 different items and subitems were evaluated independently. Further, although not an item on the REFLECT checklist (which assumes the study uses a random allocation method) it is clearly of broad interest to know if more authors are describing their allocation method. Therefore, another objective was to describe the number of studies pre- and post-2010 reporting any type of allocation method. This latter objective was not intended as an assessment of the validity of the allocation approach, i.e. not a risk-of-bias assessment; rather, the objective was only concerned with whether the authors described the method of allocation.

2. Methods

2.1. Study population

The current study was an observational survey. The population of interest was published controlled trials on naturally occurring bovine respiratory disease in weaned beef calves in Canadian and/or US feedlots. The interventions of interest were FDA-registered antimicrobials, and the outcome of interest was naturally occurring BRD (i.e., challenge trials were not relevant to this study). The study design of interest was controlled clinical trials. Our focus was further limited to journal publications, rather than technical reports or research reports, because efforts to improve reporting have mainly focused on journals.

2.2. Study selection

The literature search comprised three concepts to capture studies of interest: population, outcome, and intervention (search strings 1, 2, and 3, respectively, in Table 1) and was conducted on 15 April 2017 in MEDLINE® (Web of Science™) (Table 1) and CABI (CAB Abstracts® and Global Health®) (Web of Science™)(Supplementary material 1). Search dates were restricted to 1970–2017, with no language or document-type restrictions. All search results were exported to DistillerSR® (Ottawa, ON, Canada), where they were de-duplicated. Additionally, the reference lists of relevant reviews captured by the original search were hand-searched for potentially relevant references. Two additional relevant publications were found via a Google search while searching for PDF copies of previously identified studies. These two articles were published in *The Professional Animal Scientist* journal; therefore, the index of this journal was also searched.

Two reviewers screened each record for relevance in DistillerSR®. Eligible citations were manuscripts that described:

1) Primary research published in journals,
2) A study population of cattle housed in feedlots in Canada or the USA,
3) At least one treatment arm with a product registered with the FDA for the prevention or treatment of naturally occurring BRD, and,
4) A comparison arm (placebo or active control) i.e., controlled trials.

Two levels of screening were used to identify eligible manuscripts. The exact screening questions are presented in Supplementary material 2 and Supplementary material 3. Conflicts between reviewers were resolved by discussion or, when consensus could not be reached, by