J. Dairy Sci. 99:1–17
http://dx.doi.org/10.3168/jds.2015-9445

Invited review: Recommendations for reporting intervention studies on reproductive performance in dairy cattle: Improving design, analysis, and interpretation of research on reproduction

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ABSTRACT

Abundant evidence from the medical, veterinary, and animal science literature demonstrates that there is substantial room for improvement of the clarity, completeness, and accuracy of reporting of intervention studies. More rigorous reporting guidelines are needed to improve the quality of data available for use in comparisons of outcomes (or meta-analyses) of multiple studies. Because of the diversity of factors that affect reproduction and the complexity of interactions between these, a systematic approach is required to design, conduct, and analyze basic and applied studies of dairy cattle reproduction. Greater consistency, clarity, completeness, and correctness of design and reporting will improve the value of each report and allow for greater depth of evaluation in meta-analyses. Each of these benefits will improve understanding and application of current knowledge and better identify questions that require additional modeling or primary research. The proposed guidelines and checklist will aid in the design, conduct, analysis, and reporting of intervention studies. We propose an adaptation of the REFLECT (Reporting Guidelines for Randomized Controlled Trials for Livestock and Food Safety) statement to provide guidelines and a checklist specific to reporting intervention studies in dairy cattle reproduction. Furthermore, we provide recommendations that will assist investigators to produce studies with greater internal and external validity that can more often be included in systematic reviews and global meta-analyses. Such studies will also assist the development of models to describe the physiology of reproduction.

Key words: reporting guidelines, reproduction, study design, meta-analysis, metabolic disease definition

INTRODUCTION

Our goal is to improve the completeness, clarity, and correctness of design, analysis, reporting, and interpretation of studies on reproduction in dairy cattle. This process will improve interpretation of individual studies. More consistent and better study design and reporting will maximize the ability of researchers to use studies of reproduction in dairy cattle in systematic reviews and meta-analyses and improve understanding of the causes of variability in results from apparently similar studies.

These recommendations are directed to animal and veterinary scientists interested in improving reproductive efficiency of dairy cattle, who would use the checklists and guidelines when designing studies and preparing reports for publication. The audience includes new and established investigators, as well as reviewers and editors, who could use the guidelines to assess further the suitability of a paper for publication. We advocate that journals formally adopt the presented reporting checklist as part of the submission and review process for papers on dairy cattle reproduction.

Received February 9, 2015.
Accepted August 8, 2015.
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Suboptimal reproductive performance of dairy cattle has been well documented in economic and production system efficiency terms (Lucy, 2001; Norman et al., 2009). Reproductive performance is influenced by many factors, including genetics, young stock rearing, nutritional management, cow housing and comfort, management of the transition period, season, weather, and disease. For good reason, many of these factors have been studied in isolation, with little accounting for interacting or confounding variables, but that is changing. Research is increasingly assessing relationships for interaction and accounting for confounding of these varying effects on reproduction. Meta-analyses of nutritional effects on reproduction have been conducted (Lean et al., 2012; Rodney et al., 2015), identifying a negative effect of soluble protein and positive effects of fatty acids on reproductive performance in lactating dairy cows, respectively. Several systems models of reproduction and the integration of genetics, nutrition, and reproduction have been recently published (Boer et al., 2011; Martin et al., 2012; McNamara and Shields, 2013).

The low estimates of heritability of reproductive performance reflect the fact that fertility traits are complex and multifactorial; however, the estimated genetic merit for reproductive traits is increasing (Berry et al., 2014). Important explanatory environmental variables; that is, nongenetic effects that influence reproduction, are unmeasured in most genetic analyses and most physiology and nutrition experiments. Numerous environmental variables likely contribute considerably more compared with genetics to reproductive phenotype directly (Bello et al., 2012). The environmental effects that need to be accounted for might be poorly and inconsistently measured, and definitions of fertility measures can vary. Such problems lead to the possibility of substantial unmeasured genotype by environment interactions. The compilation of studies for further detailed analyses by systematic review or meta-analysis may help to identify the presence and sources of heterogeneity of results among investigations of a similar research question (Bisinotto et al., 2015), but only if the primary studies are sufficiently valid, completely reported, and consistent in definitions and conduct to be included; unfortunately, this is rarely the case (Haimerl et al., 2013; Rodney et al., 2015).

Relatively few recent publications have addressed study design in cattle research using randomized controlled trials, but examples include St-Pierre (2007) and Tempelman (2009). Those authors stressed the need for adequacy of sample size and the need to avoid pseudo-replication, and they discussed appropriate approaches to study design. In conducting meta-analyses on reproductive studies examining hormonal and dietary interventions, the following failings were noted in many of the studies evaluated: randomization or allocation methods were not described; the blinding of researchers to treatment allocation was not stated; the use of placebo treatments was not stated; some studies lacked clarity in regard to whether nutritional treatments were allocated to individual cattle or groups of cattle; and relatively few papers provided or correctly analyzed time-to-event outcomes; for example, time to first service or pregnancy (Amann, 2005; Haimerl et al., 2013; de Boer et al., 2014; Rodney et al., 2015). Finally, notwithstanding earlier attempts to standardize reporting of reproductive outcomes (Fetrow et al., 1990), there has been inconsistent use of outcome measures and terminology in studies of reproductive performance. These failings are not unique to reproductive studies; others have documented deficiencies in study design and reporting in human and veterinary medicine (DerSimonian et al., 1982; Elbers and Schukken, 1995; Moher et al., 2001; O'Connor, 2010). Further, the problems of reproductive research study design are not isolated to cattle (Kastelic and Gandolfi, 2005). Substantial flaws in reproductive study design for studies involving horses, cattle, swine, companion, laboratory, and wild animals have been noted (Amann, 2005; Simoneit et al., 2011). The need to use research resources efficiently and to maximize the information gleaned from experiments on reproductive performance of dairy cattle provided the major stimulus to develop these guidelines. Reporting guidelines are one useful tool to improve the quality of published research (O'Connor, 2010). The "CONSORT statement," checklist and explanation document (Consolidated Standards of Reporting Trials; Moher et al., 2001) was developed primarily for human medicine to provide guidelines for design, conduct, and reporting of randomized controlled trials and contain standard methods and guidelines for reporting measures. Veterinary medical and food safety specialists adapted CONSORT to produce the "REFLECT statement" on Reporting Guidelines for Randomized Controlled Trials (O'Connor et al., 2010; Sargeant et al., 2010) for livestock trials, and guidelines for animal research have also been produced (Kilkenny et al., 2010). Papers in medical journals that endorse the CONSORT guidelines have more complete reporting of randomized controlled trials, although after many years, there is still room for improvement (Turner et al., 2012).

A CHECKLIST AND GUIDELINES FOR STUDIES IN DAIRY CATTLE REPRODUCTION

Awareness of the limitations in the capacity of any individual research group to address the challenges of improving reproductive performance of cattle grew